The National Academies of
SCIENCES · ENGINEERING · MEDICINE



Good Clinical Laboratory Practices in Pakistan

Editors:
Aamer Ikram, Rita Guenther and Benjamin Rusek

GOOD CLINICAL LABORATORY PRACTICES IN PAKISTAN

2019

Pakistan Academy of Sciences

in collaboration with

The National Academies of SCIENCES ENGINEERING MEDICINE

(NASEM)

Editors
Aamer Ikram, National Institute of Health, Pakistan
Rita Guenther and Benjamin Rusek, NASEM, United States

THE PAKISTAN ACADEMY OF SCIENCES

This activity was supported by the Pakistan Academy of Sciences, the U.S. National Academies of Sciences, Engineering, and Medicine, and the U.S. State Department. The Pakistan Academy of Sciences is solely responsible for this publication and the contents are the responsibility of the individual chapter authors.

International Standard Book Number-13: 978-0-578-46481-7

Additional copies of this report are available from the Pakistan Academy of Sciences.

Copyright 2019 by the Pakistan Academy of Sciences. All rights reserved.

Suggested Citation: Pakistan Academy of Sciences. 2019. Good Clinical Laboratory Practices in Pakistan. Islamabad, Pakistan.

Printed by Shiuman Design & Print, Blue Area, Islamabad-Pakistan
Price: $15; PKR 1500

Preface & Acknowledgements

The *Handbook for Good Clinical Laboratory Practices in Pakistan*, created by the Pakistan Academy of Sciences (PAS) in collaboration with the U.S. National Academies of Sciences, Engineering, and Medicine (NASEM), is intended to serve as an informational guide for clinical laboratories in order to improve the health and wellbeing of people and animals in Pakistan.

Promotion of laboratory best practices and communication between and among laboratories is the best way to enhance disease surveillance and to help establish the relationships that keep experts engaged with the international community of responsible practitioners working for the public good. Ultimately, the creation of this handbook is a starting point to continue the discussion and evolution of creating and implementing best practices within clinical laboratories. PAS and NASEM hope that the content will be useful to the thousands of dedicated men and women supporting the people, animals, plants, and environment of Pakistan in the spirit of “One Health” and in some way, lead to a strengthening of the population of talented humans responsible for the health and well-being of the citizens of Pakistan.

Each of the 25 chapters in the handbook focuses on a common issue and/or process faced by those working in the wide range of clinical laboratories across the country. The information in the handbook was provided by a diverse and highly talented group of laboratory leaders, scientists, and experts, their names and affiliations are listed on the title page of each chapter. Without their wisdom, experience, and hard work the handbook would not have become a reality.

The preparation of this handbook was a true collaboration between PAS and NASEM. The initial concept and vision for the project came from Dr. Anwar Nasim, President of PAS at the time of project initiation. Dr. Nasim suggested that PAS and NASEM work together to develop a document to strengthen Pakistani laboratories, human and veterinary, throughout the country. Professor (Dr.) Aamer Ikram, now the Executive Director of the National Institute of Health, Islamabad, took the lead in coordinating the effort in Pakistan from concept development to the final published product. In April of 2017, Dr. Ikram and then PAS Secretary General, Dr. Zabta Shinwari held a meeting in Islamabad with NASEM staff to discuss the handbook, meet with potential chapter authors, and plan the project. Under Dr. Ikram's leadership, a small team from PAS and NASEM developed the goals, proposed content for the handbook, and met with potential chapter authors. Pakistani scientists and clinicians, selected by the joint team, then developed initial drafts of all the chapters. A small group of U.S. scientists and clinicians served as co-authors, reviewing and contributing thoughts to the drafts. After the chapter authors completed their initial drafts, PAS and NASEM organized a workshop in January 2018 in Bangkok, Thailand designed to allow the chapter authors to present and discuss their draft chapters with the other chapter authors and assembled experts. Project leaders used the input from this workshop to construct the final version of the handbook. In producing the final draft, the project leaders and chapter authors drew on data gathered during a 2016 PAS and NASEM workshop on promoting best practices in and improving communications, cooperation, and coordination among public, private, and animal health clinical laboratories in Pakistan. Although the handbook is the result of a collaborative process between PAS appointed Pakistani chapter authors and NASEM

appointed experts in the United States, PAS is solely responsible for this publication and each chapter is the responsibility of the individual author or authors.

As PAS and NASEM have worked together, communicating, writing and editing we have created a positive and productive community of understanding. PAS and NASEM thank Dr. Nasim and Dr. Shinwari for the PAS's broad support and encouragement. We thank Mr. Adnan Bashir, of the PAS and NIH staff for their administrative support. We are grateful to Dr. David Franz, Dr. Rita Guenther, and Mr. Benjamin Rusek for their contributions from the NASEM and to Dr. Krista Versteeg also from the NASEM for editorial support. Special thanks goes to Dr. Ikram for the many hours spent guiding the authors along the journey and for his absolutely critical substantive and editorial contribution to the final handbook.

The diverse and highly talented group of authors and co-authors shared their wisdom, experience and hard work for making this manual a reality. We are thankful to Dr. Kahlid Naeem for covering veterinarian aspects of laboratories under 'one health' concept.

Although the first edition of the written handbook is designed to help the Pakistani laboratory community strengthen their practices, PAS intends for the handbook to be a “living document” to allow for revisions as technology and best practices change. The handbook will be printed and widely distributed and is posted on the websites: PAS (www.paspk.org/); and NIH (www.nih.org.pk/). Future editions may be produced as a web application for easier viewing by smartphone users.

Prof. Zabta Khan Shinwari
Ex-Secretary General
Pakistan Academy of Sciences

Prof. Muhammad Qasim Jan
President
Pakistan Academy of Sciences

Forward

Clinical laboratories are considered an indispensable and fundamental component of the health system and contribute directly to the improvement of health services delivery. Accurate, reliable and timely results from laboratory investigations are critical elements in decision-making in clinical settings. From the public health perspective, critical decisions concerning health security, diseases surveillance, response, outbreak detection and meeting international obligations, such as the International Health Regulations (IHR) 2005, also depend upon reliable laboratory services.

As part of a multi-year project to promote a cooperative relationship between Pakistani and American health and infectious disease experts, the Pakistan Academy of Sciences (PAS), together with the U.S. National Academies of Sciences, Engineering, and Medicine (NASEM) has produced this handbook for improving laboratory services in Pakistan with a special focus on raising the quality and capabilities of laboratories functional even in the remotest areas of the country.

This laboratory manual has been developed covering all key aspects of laboratory operations and functions, under a 'One Health' concept. It has been written with developing countries context, providing simple and hands-on guidance on pre-analytical, analytical and post analytical components of the laboratory operations. The manual has been drafted through a consultative process involving various subject matter experts thereby consolidating a vast range of knowledge and experience.

The first edition of this *Handbook for Good Clinical Laboratory Practices in Pakistan* will be a helpful guide and reference not only for the beginners but mid to higher tiers as well as specialists in various laboratory disciplines. The main concept was to cover up all those deficient areas not covered under different curricula. The content aims to address some of the laboratory associated challenges in developing countries along with their practical solutions. The manual provides guidelines for establishing laboratory management, laboratory operations, and quality management systems. The manual covers a broad range of topics including facility design, biorisk management, data management and networking, laboratory quality management system, contingency planning, surveillance & reporting and laboratory leadership. As such it will remain an asset for all the biomedical laboratories besides clinical side. This handbook will eventually be published in local languages and promoted and disseminated across Pakistan.

Prof. Dr. Aamer Ikram, SI(M)
Executive Director
National Institute of Health

Summary

The *Handbook for Good Clinical Laboratory Practices in Pakistan* is divided into four sections based on overarching themes: laboratory management, laboratory safety, laboratory operations, and quality management systems. Each of the sections is divided into chapters that provide standard information on best practices and specific suggestions that will assist individuals in the clinical laboratory setting. Additionally, the handbook contains appendices that help to elucidate various aspects of laboratory duties and tasks as well as useful definitions that are commonly used in the workplace.

In Section I, Lab Management, the chapters cover the role of leadership; best practices in laboratories; training, certification, and continuing education of personnel; laboratory design guidelines; and budgeting and sustainability issues. In the first chapter, the authors highlight the need for strong and steady leadership to create an environment that helps to build upon their team's strengths by ensuring that the hiring of staff is professionally driven and a culture of trust is cultivated. Chapter 2 begins by outlining the key components of best laboratory practices. Those components, which include proper documentation and method validation, provide the foundation for ethics and professionalism in the laboratory. The importance of continuing professional development for laboratory employees is the major theme in Chapter 3, and the authors outline specific activities for the laboratory staff to increase their proficiency of technical skills and identify knowledge gaps. In Chapter 4, the author describes the guidelines for laboratory design, which include commissioning, and concepts of containment to create safe and sound laboratory working environments, designed to easily evolve over time to fit the needs of laboratory staff. The chapter includes detailed recommendations for building construction materials to be used, furniture requirements, proper ventilation, and other recommendations to keep personnel safe from the materials being handled. Budgeting and financial issues important to running a sustainable laboratory are described in Chapter 5. Laboratory equipment standardization is noted as a means of ensuring that standard results are administered by each laboratory.

Section II covers laboratory safety essentials related to occupational health; safety systems and safety culture; biosecurity; biorisk management; and emergency responses and preparation for common emergencies. This section delves into the importance of training staff and personnel to understand the risks of handling dangerous substances. Chapter 6 provides an introduction to laboratory safety measures that are important to reduce the number of laboratory accidents and includes information on how individuals should respond when a situation of concern arises. Regular risk identification and assessment exercises are noted as a means of reducing harmful incidents and ensuring that personnel are capable of handling hazards safely when they happen. Moreover, the chapter outlines preventative measures to protect individuals from suffering laboratory-acquired infections through the use of personal protective equipment, and ensuring that all staff are properly trained in up-to-date safe practices. The next chapter describes laboratory safety systems and safety culture in more detail, and discusses knowledge management systems that can help inculcate behavioral changes to effectively implement safety culture into an organization. Chapter 8 discusses the important work that biomedical laboratories do to protect society from emerging and re-emerging infectious diseases, and explains the importance of implementing good biosecurity

measures to prevent biological disease outbreaks or bioterrorism. The chapter notes that a biosecurity plan is only the first step and that continual evaluation and assessment of the management system is essential to help improve the safety of the laboratory and protect its personnel from threats. Even with the best preparation and pre-planning, emergencies can happen, and laboratory personnel need to be prepared to handle any issue. Chapter 9 introduces biorisk assessment and mitigation concepts, discusses the components of risk assessment, and provides a review of the methods for performing risk assessments. In Chapter 10, the authors discuss the importance of an emergency response plan and identify the different phases within a plan: mitigation, preparedness, response, and recovery. Each phase requires a specific set of tasks designed to minimize the severity of the emergency. Additionally, this chapter outlines the types of laboratory accident categories and the appropriate response to each.

In Section III, Laboratory Operations, the chapters cover the administrative, data-management, and communication aspects of laboratories. Preparation of a procedure manual, described in Chapter 11, allows for clear and concise guidelines for laboratory personnel. Each laboratory will have different requirements, but a manual for each procedure should include general information such as a list of basic equipment, laboratory rules, details on clean up, and other information, including clinical pathology and specimen procedures. Chapter 12, on laboratory waste management, includes a discussion on proper waste disposal methods for high hazard waste and material. Communication, data sharing, and networking are key components of public and private healthcare systems and clinical laboratories. Chapter 13 describes networking; provides an overview of data sharing and reporting systems in Pakistan, identifies the best ways to communicate results from field collection and laboratory reports, and urges the creation of uniform measures to communicate via new technologies. Chapter 14 discusses information management systems. The author describes a successful electronic laboratory information system as one that has standard fields that can lead to error reduction, easy access to information and data sharing for the user, and the ability to create standard reports and records. Standard data collection, sharing and reporting serves to help public health officials detect and combat infectious disease outbreaks. Disease outbreak prevention is further covered in Chapter 15, in which the author describes the role of laboratories in disease surveillance, and detection as the best way to protect the broader population in Pakistan in health emergencies. Chapter 16 describes components of a sample management system that help to maintain a safe environment for laboratory personnel. The author stresses the importance of sample management through a sample inventory system to ensure that samples involving potentially hazardous biological materials (such as those that harbor human and animal pathogens) are handled in a manner such that research personnel, support staff, the public, and the environment are not exposed. Chapter 17 addresses specimen transportation or shipment and outlines practices to facilitate the transportation of infectious, diagnostic and exempt substances whether by post, road, sea, rail, or air. Chapters 18 and 19 examine equipment performance as it relates to quality assurance, and troubleshooting methods when equipment failures occur. The chapters focus on the need for accurate documentation to assess the fitness of the equipment and when to retire older laboratory equipment.

The final section, Quality Management System, describes the importance of standards within laboratories; quality control; occurrence management; method validation; and laboratory certification and accreditation. Chapter 20 identifies laboratory standards that are periodically reviewed and redefined as an essential aspect of good laboratory management. The author has identified laboratory aspects that should use a standardized approach: management, technical, personnel, laboratory information systems, documentation, equipment, and quality management. Quality control and quality indicators that help define and measure progress and minimize laboratory errors are discussed in Chapters 21 and 22. In these chapters, the authors describe the types of quality control systems ensuring that laboratory results are accurate, reliable, and consistent. The authors of Chapter 23 provides laboratory personnel with a systematic approach to reduce errors and resolve common issues through occurrence management practices. In Chapter 24, the authors further outline how to reduce errors using method validation, which is the process to determine whether an error might be present in a laboratory test result. Chapter 25 discusses obtaining laboratory certification and personnel accreditation, which are additional components in operating a safe and reliable laboratory. Each of the certifications ensures that the laboratory is functioning in accordance with accepted norms.

The Handbook appendices provide further detail and explanation of laboratory and scientific terminology and techniques, and examples of common documents that are used in the laboratory. Appendix 1 provides suggested abbreviations for different units of measurement. A list of reportable diseases in Pakistan, which was developed by the Federal Ministry of National Health Services; Regulations and Coordination can be found in Appendix 2. In Appendix 3, the authors have created a sample job description to attract qualified laboratory personnel. Appendices 4 and 5 address hazard identification and material safety to ensure that personnel handle potentially dangerous substances safely and securely. The list (Appendix 4) helps to identify risks associated with temperature and hazardous environments. The materials safety data sheet (Appendix 5) explains how to work safely with common laboratory materials. Appendix 6 lists the contact information of pathology and diagnostic laboratories within Pakistan. Appendix 7 lists infectious substances and their corresponding shipping identification numbers. A sample equipment logbook entry table is detailed in Appendix 8, and is designed to help lab employees track the equipment's status over a period of time. Appendix 9 provides an example of an incident notification form in cases of emergency or accident in the laboratory. A laboratory inventory sheet is included as Appendix 10 and is designed to help personnel clearly identify what and where a substance is physically located in the laboratory. Appendix 11 describes SOPs for some of the common laboratory procedures for dealing with human biological samples. Definitions of common terminology used in laboratories are provided in Appendix 12.

Table of Contents

Summary	iv
SECTION I: LABORATORY MANAGEMENT	xix
Chapter 1: The Role of Leadership in Diagnostic Laboratories	**1**
Muhammad Tahir Khadim, Armed Forces Institute of Pathology, Rawalpindi; Anwar Nasim, Pakistan Academy of Sciences; David Franz, U.S. Army Retired	1
Defining the Role of Leaders	1
Vision and Mission	1
Emotional Intelligence	2
Guidelines for Building a High-Performance Laboratory Team	3
Staffing of the Diagnostic Laboratory and Guiding Principles	3
Staff Development and Continuing Professional Development	5
The Work-Life Balance	5
Effective Communication With Laboratory Staff	5
Gender Equality and Cultural Challenges	6
Change and Innovation	6
Communication and Information Technologies	7
Quality Management	7
Planning and Budgeting	8
Laboratory Safety and Security	8
The Power of Communities of Trust	9
Bibliography	9
CHAPTER 2: BEST LABORATORY PRACTICES	**10**
Ayesha Junaid, Shifa College of Medicine; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory; Muhammad Tahir Khadim, Armed Forces Institute of Pathology, Rawalpindi	10
Definition	10
Best Laboratory Practices	10
Ethics and Professionalism	14
Essentials of Ethics and Professionalism	15
Essentials Components of Professionalism	15
How To Learn Professionalism?	17
Principles of Professionalism in Healthcare Professions	15

Commitments of Professionalism 17
Key Elements of Professionalism 18
Further Readings 19
Bibliography 19
CHAPTER 3: TRAINING, CERTIFICATION AND CONTINUING EDUCATION OF CLINICAL LABORATORY PERSONNEL GENERAL PRINCIPLES 20
Muhammad Tahir Khadim, Armed Forces Institute of Pathology, Rawalpindi; Maureen Sullivan, Minnesota Public Health Laboratory 23
Continuing Professional Development 23
Bibliography 25
CHAPTER 4: LABORATORY DESIGN GUIDELINES 25
Uzma Bashir Aamir, National Institute of Health, Islamabad; David Franz, U.S. Army Retired 25
Laboratory Commissioning and Commissioning Agents 25
The Concept of Laboratory Containment 28
Basic Principles in Clinical Laboratory Design 30
Key Elements of Laboratory Layout/Design Planning 31
Recommendations for Laboratory Construction/ Renovation Materials 32
Equipment Zones 33
Laboratory Furniture Requirements 33
Mobile Casework/Cabinets 33
Laboratory Storage Space 33
Flexible Engineering Systems 34
Laboratory Ventilation 34
Specific Ventilation Equipment 35
Laboratory Support Areas/Specialized Areas 37
Specialized Areas 38
Sustainability In Laboratory Design 38
Relevant Codes And Standards 39
Bibliography 40
CHAPTER 5: BUDGETING AND SUSTAINABILITY ISSUES 41
Ghulam Sarwar Pirkani, Bolan Medical College; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 41

Standardization and Harmonization 41
Laboratory Consumables Management 43
National Procurement Committee 43
Bibliography 45
SECTION II: LABORATORY SAFETY 47
CHAPTER 6: LABORATORY SAFETY ESSENTIALS: OCCUPATIONAL HEALTH AND SAFETY, VACCINES, PERSONAL PROTECTION AND AVOIDING LABORATORY ACQUIRED INFECTIONS (LAIS) 49
Nasrullah Malik, Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore; Yasir Rafiq, Combined Military Hospital, Skardu 49
Guides to Potential Hazards 50
Spill Kits 50
Chemical Safety 51
Limit and Control of Hazards 51
Bio-Incident 51
Biosafety 51
Biosecurity 51
Biological Risk Mitigation 52
Risk Identification 52
Risk Assessment 54
Risk Based Classification Of Microorganisms 54
Mitigation Measures – Reducing The Impact 55
Occupational Health Safety 56
Medical And Incident Surveillance 57
Vaccines 58
Laboratory Acquired Infections And Prevention 58
Safety Equipment and Personal Protective Equipment 69
Eye And Face Protection 61
Lab Coats And Aprons 61
Gloves 61
Foot Protection 62
Respiratory Protection 62
Hand Washing 62
Training For Laboratory Personnel 63

Immunization 63
Protection From Sharps 63
Biosafety Cabinets 64
Other Essentials 64
Bibliography 64
CHAPTER 7: SAFETY SYSTEMS AND SAFETY CULTURE 65
Tim Trevan, Chrome Biorisk Management Consulting, U.S. 65
Introduction 65
Safety and Systems 65
The Limits of Knowledge 68
Safety and Culture 69
Bibliography 71
CHAPTER 8: BIOSECURITY 72
Shamsul Arfin Qasmi, Karachi Institute of Medical Sciences Julie Pavlin, National Academies of Sciences, Engineering, and Medicine, U.S. 72
Introduction 72
History of Bioterrorism 72
Definition of Biosecurity 73
Identification of Valuable Biological Material (VBM) 73
Risk Assessment 74
Definitions 74
Fundamentals of Biosecurity 75
Program Management 76
Recommendations 76
Emergency Response Force 77
Testing Of Performance And Documentation 77
Training 85
Necessity For Biosecurity 78
Bibliography 78
CHAPTER 9: BIORISK MANAGEMENT: BASIC CONCEPTS & ASSESSMENT TOOLS 80
Erum Khan and Sadia Shakoor, Aga Khan University, Karachi 80
Biorisk Assessment and Mitigation 80

Components of Risk Assessment 80
Tools & Techniques for Performing Risk Assessments 83
Bibliography 88
CHAPTER 10: EMERGENCY RESPONSE FOR LABORATORIES: AN OUTLINE FOR PREPARATION IN COMMON EMERGENCIES 89
Faisal Hanif, Bahria University Medical & Dental College; Umar Khurshid, Armed Forces Institute of Pathology; Maureen Sullivan, Minnesota Public Health Laboratory 89
Emergency Plans 89
Major Laboratory Accidents 93
Occupational Health Program And Medical Surveillance Program 99
Accidents, Incidents, Near Misses And Undesired Circumstances 100
Bibliography 101
SECTION III: LABORATORY OPERATIONS 103
CHAPTER 11: PREPARATION OF PROCEDURE MANUALS 105
Irfan Ali Mirza, CMH Lahore Medical College 105
Introduction 105
Beneficiaries Of Procedure Manual 105
Advantages Of Procedure Manual 105
Requirements Of A Procedure Manual 105
Practical Instructions For Manual 106
Bibliography 110
CHAPTER 12: LABORATORY WASTE MANAGEMENT 111
M. Asghar Javaid, Nishtar Medical College, Multan; Affan Shaikh, U.S. 111
Types of Wastes 111
Identifying Hazardous Wastes 112
Four Primary Waste Disposal Techniques 112
Waste Minimization 113
Waste Preparation 113
The Labelling of Waste 113
Colour Code for Segregation of Waste Material 114
Infectious Waste 115
Disposal of Waste 115
Materials and Equipment 115

Waste Streams associated with the Laboratory 115
Autoclaving 117
Incineration 118
Shredding 118
PPE 118
Waste Management: Everyone's Responsibility 118
Responsibilities for Waste Management 119
The Hospital Must Provide 119
Bibliography 120
CHAPTER 13: NETWORKING, DATA SHARING AND COMMUNICATION 121
Muhammad Usman, Shifa International Hospital, Islamabad; Affan Shaikh, U.S. 121
Laboratory Networking 121
Laboratory Data Sharing 122
Reporting of Communicable Infections 123
Bibliography 124
CHAPTER 14: LABORATORY INFORMATION MANAGEMENT 125
Muhammad Usman, Shifa International Hospital, Islamabad; Affan Shaikh, U.S. 125
Introduction 125
Elements Of Lab Information System 125
Procedure To Assure Accuracy Of Data Recording, Reporting And Communication 128
Information Security, Storage And Confidentiality 129
Manual Paper-Based Systems 130
Computerized Laboratory Information Systems (LIS) 131
Bibliography 134
CHAPTER 15: SURVEILLANCE, REPORTING AND REFERRAL OF SPECIMENS 135
Muhammad Salman, National Institute of Health, Islamabad Ali S. Khan, University of Nebraska Medical Center, Omaha 135
Surveillance 135
Public Health Testing 136
Health Laboratory Services 136
Laboratory-Based Surveillance 136
Role of Laboratories In Disease Surveillance 137

Elements of Laboratory Based Surveillance System 138
Establishing Laboratory Support for Public Health Surveillance 139
Bibliography 141
CHAPTER 16: SAMPLE STORAGE AND ARCHIVING 143
Muhammad Salman and Muhammad Masroor Alam National Institute of Health, Islamabad 143
Introduction 143
Importance of Good Sample Management and Its Role in Laboratory Quality Management System (LQMS) 143
Components of a Sample Management System 144
Implementation of a Laboratory Inventory Management System 144
Sample Referral to Allied Laboratories and Collaborators 146
Main Considerations for Laboratory Inventory Management System 147
Template of Sample Inventory 147
Labelling of Storage Vials 147
Long-Term Storage Of Samples At -80°C Freezer 148
Inventory Management Software 148
Bibliography 148
CHAPTER 17: SHIPMENT/TRANSPORT OF SPECIMENS 149
Shamsul Arfin Qasmi, Karachi Institute of Medical Sciences, Pakistan Julie Pavlin, National Academies of Sciences, Engineering, and Medicine, U.S. 149
Introduction 149
Definitions 149
Category A (Infectious Substances) 149
Category B (Biological Substances) 149
Exempt Substances 149
Taxonomy & Characterization 150
Medical/Clinical Waste 150
Shipping Regulations 150
Steps for Packaging Samples 154
International Regulations 154
National Regulations 155
Shipping In Pakistan 155
Bibliography 156

CHAPTER 18: EQUIPMENT PERFORMANCE IN RELATION TO QUALITY ASSURANCE **157**

Ashok Kumar Tanwani, Pakistan Institute of Medical Sciences; Muhammad Yousaf Janjua, Pakistan Institute of Medical Sciences, Islamabad; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 157

Scope 157

Selection Of Equipment 157

Installation of Equipment 158

Getting the Equipment Ready for Service 158

Implementation of Equipment Maintenance Programme 159

Quality Control 160

BIBLIOGRAPHY 161

CHAPTER 19: TROUBLESHOOTING, SERVICE, REPAIRING AND RETIRING THE EQUIPMENT **162**

Ashok Kumar Tanwani, Pakistan Institute of Medical Sciences; Muhammad Yousaf Janjua, Pakistan Institute of Medical Sciences, Islamabad; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 162

Source of the Problem 162

Troubleshooting 162

When Problems Are Not Resolved 162

Service And Repair 163

Retiring And Disposing The Equipment 163

Documentation Of Equipment Maintenance 163

Bibliography 164

SECTION IV: QUALITY MANAGEMENT SYSTEM 165

CHAPTER 20: STANDARDS IN CLINICAL LABORATORIES **166**

Ayesha Junaid, Shifa College of Medicine; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 166

Standards 166

Laboratory Standards 166

Technical Standards 167

Bibliography 170

CHAPTER 21: QUALITY CONTROL IN MICROBIOLOGY LAB **171**

Irfan Ali Mirza, Combined Military Hospital Lahore Medical College 171

Introduction 171

Quality Control Parameters 171
QC Program In Microbiology Lab 172
Assessment of Quality 174
Bibliography 175
CHAPTER 22: QUALITY CONTROL 176
Aamir Ijaz, Rehman Medical Institute, Peshawar; Muhammad Rafi Butt, MedAsk Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 176
Terminology 176
Types Of QC 176
Choice of the QC Materials 177
Some Basic Statistics 177
Proficiency Testing 178
Objectives of EQA Schemes 178
International EQAS Available In Pakistan 179
National External Quality Assurance Programme In Pakistan (NEQAPP) 179
Bibliography 180
CHAPTER 23: OCCURRENCE MANAGEMENT 181
Aamir Ijaz, Rehman Medical Institute, Peshawar; Muhammad Rafi Butt, MedAsk Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 181
Laboratory Errors 181
Difference Between Precision And Accuracy 182
Shift and Trend 182
Principles of Trouble Shooting 183
Delta Check 185
Bibliography 187
CHAPTER 24: METHOD VALIDATION 188
Aamir Ijaz, Rehman Medical Institute, Peshawar; Ayesha Junaid, Shifa College of Medicine, Islamabad; Muhammad Rafi Butt, MedAsk, Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 188
Introduction 188
Terminology 188
Characteristics to Be Considered For Selection of a Routine Test 188
Laboratory Studies Required For Method Validation 191
Bibliography 192

CHAPTER 25: LABORATORY CERTIFICATION & ACCREDITATION **193**

Aamir Ijaz, Rehman Medical Institute, Peshawar; Ayesha Junaid, Shifa College of Medicine, Islamabad; Muhammad Rafi Butt, MedAsk, Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory 193

Certification vs Accreditation 193

Accreditation Of Clinical Laboratories (Medical and Veterinary) 193

Why Accreditation? 193

Accreditation Initiative At National Level 193

Accreditation Bodies 194

Accreditation Standards 194

Proficiency Testing (PT) Is a Must for Lab Accreditation 194

Accreditation Is Recognition 194

Initiative for Accreditation 194

ISO 15189 Overview 195

Documentation of the System 197

Common Mistakes While Documenting Systems 198

How To Get Accredited 198

Bibliography 199

APPENDIX 1: UNITS OF MEASURE **201**

Faisal Hanif, Bahria University Medical College; Umar Khurshid, Armed Forces Institute of Pathology, Rawalpindi 201

References 202

APPENDIX 2: LIST OF REPORTABLE DISEASES **203**

Uzma Aamir, National Institute of Health, Islamabad 203

Annexure: Reportable Diseases 203

1. Priority Diseases 203

2. Zoonotic Priority Diseases 203

Old Classification of Diseases Notifiable to the OIE 204

APPENDIX 3: SAMPLE JOB DESCRIPTION **208**

Faisal Hanif, Bahria University Medical College; Umar Khurshid, Combined Military Hospital, Khuzdar Cantt 208

Headings for Individual Job Description 208

APPENDIX 4: WORK PLACE HAZARD IDENTIFICATION **211**

APPENDIX 5: MATERIAL SAFETY DATA SHEET **213**
Faisal Hanif, Bahria University Medical College; Umar Khurshid,
Armed Forces Institute of Pathology, Rawalpindi 213
Information on MSDS 213
Product Information 213
Hazard Identification 214
Ingredients 214
First Aid 215
FireFighting 215
Accidental Release 215
Storage And Handling 215
Personal Protection 216
Physical and Chemical Properties 216
Stability 217
Toxicology Information 217
Sample MSDS Data Sheet 218
References 218
APPENDIX 6: IMPORTANT CONTACTS **219**
APPENDIX 7: SHIPPING INFORMATION **223**
Shipping Identification numbers: 224
APPENDIX 8: EQUIPMENT LOGBOOK **225**
APPENDIX 9: INCIDENT NOTIFICATION FORM **226**
APPENDIX 10: EXAMPLE OF INVENTORY SHEET **227**
APPENDIX 11: SOPS FOR LABORATORY PROCEDURES **229**
Some Examples 229
Stool Routine Examination 229
SOP for Blood CP 231
SOP for Haematoxylin and Eosin Staining 234
Haematoxylin and Eosin Staining 234
APPENDIX 12: DEFINITIONS **237**
Important National Documents 241

SECTION I:
LABORATORY MANAGEMENT

Chapter 1

The Role of Leadership in Diagnostic Laboratories

Muhammad Tahir Khadim, Armed Forces Institute of Pathology, Rawalpindi;
Anwar Nasim, Pakistan Academy of Sciences; David Franz, U.S. Army Retired

"**A leader is one who knows the way, goes the way, and shows the way**."
John C. Maxwell

DEFINING THE ROLE OF LEADERS

Leadership defines vision and motivation for all members of the organization to achieve the goals of the organization. Leadership in general sets directions and provides the platform to move the organization in right direction. There can be different models of leadership in various contexts. Informed and engaged leadership is central to the success of a diagnostic laboratory. To achieve the maximum healthcare goals, diagnostic laboratories are organized to assure that the team is greater than the sum of its component parts. Enlightened leadership can guide a laboratory team to achieve and perform beyond its expected capabilities. A leader's job is not only to control but also to teach, encourage, organize and facilitate. Effective leaders have technical insight regarding all the aspects of diagnostic operations, the work environment, equipment maintenance, quality and reliability of results and the confidence of all of the laboratory's stakeholders. An effective leader need not be as technically competent as the team's subject matter experts but is comfortable leading experts more accomplished. The topics of this chapter include the various aspects of a leader's role in a diagnostic laboratory, both at the primary and tertiary healthcare levels as well as in referral laboratories.

VISION AND MISSION

A leader must have a vision for the laboratory's mission accomplishment and clearly elucidate that vision to other members of the organization. While defining the laboratory's vision, it is important to clearly explain the primary purpose of the diagnostic laboratory which is to provide accurate, reliable and timely results to clinicians, thereby having direct positive impact on the management of each individual patient and promotion of health more broadly at all levels of the medical enterprise. Day to day activities of the staff also include the required technical improvements, elimination of possible errors through quality control, improvement of assay protocols, continual efforts to update the lab's technical hardware and staying abreast of innovation in health services. Leaders should encourage a culture of thinking in terms of "continual quality improvement". In addition to professional development of the staff, measures of success and rewards for excellent performance are the responsibility of an excellent leader. Every leader needs technical competence, but technical expertise alone is not enough.



FIGURE 1-1: Laboratory leadership components (author's graphic)

EMOTIONAL INTELLIGENCE

Increased technical complexity and ever-changing healthcare management practices have significantly impacted the role of medical laboratories. Laboratory leaders must be able to explain such changes to laboratory staff, healthcare workers and patients. Lundberg stated in 1999, “The personal interaction between physicians and laboratorians has increased drastically since 1990 and will continue to increase as the value of the clinical laboratory and those who staff it expands”. This challenge is relevant to the laboratory director and will require increased interpersonal communication and mastery of soft skills. Unfortunately, not all technically competent healthcare professionals have spent time honing their soft skills, which are so necessary for effective human interaction.

An important role of the leader is to help instill traits such as collaboration, mutual trust, empathy, genuine appreciation, honesty and passion in the hearts and minds of the staff. Developing common work ethics and defining and setting a moral compass for the team is as essential as sophisticated reliable, up to date diagnostic equipment in the laboratory. Leaders, through their emotional intelligence, can inculcate the culture and improve the work environment with all these ingredients. A leader will point out opportunities for improvement when 'teaching moments' present themselves but do so in a positive manner so as not to undermine workers' confidence or the drive to grow and succeed. A few specific guidelines that illustrate the most necessary soft skills and approaches to implementing them effectively are elaborated here.

GUIDELINES FOR BUILDING A HIGH-PERFORMANCE LABORATORY TEAM

Team members respond to observed actions better than to verbal orders. Like an efficient and trustworthy team in any field of endeavor, the following are some key guiding points for developing an effective diagnostic laboratory. These points are emphasized in relevant sections of this chapter.

- Define a very clear picture of the healthcare or diagnostic requirements: a vision for the team.
- Establish clear goals in terms of technical diagnostic capabilities and contributions towards patient management.
- Communicate with staff frequently, particularly in difficult or controversial situations.
- Build and maintain trust at all levels by encouraging accountability of each team member and by operating in a way that earns the trust of the team.
- Maintain unity and discipline among all categories of the laboratory staff.
- Always be a good listener; let others speak freely.
- Make decisions and take informed risks.
- Provide candid and constant feedback.
- Learn to recognize and provide opportunities to grow and accept more responsibility, especially in the case of talented team members.
- Reward good performance, human interaction and behavior.
- Take every opportunity to encourage pleasant learning experiences.
- As a leader, be confident and dependable.
- Create opportunities to make the work environment enjoyable for all.
- Focus on the collective mission.

STAFFING OF THE DIAGNOSTIC LABORATORY AND GUIDING PRINCIPLES

Every organization comprises human resources who come and go throughout the life of the organization. Staff hiring and retention, to enhance mission and goals of the diagnostic laboratory, are never ending important and challenging tasks for a leader. The Human Resources department must always seek guidance from the technical managers. Overstaffing or understaffing can reduce the effectiveness of the organization. The following cardinal principles can serve as guiding points for strategic hiring:

- **Timing for laboratory staff hiring:** Practices vary in different healthcare systems. Usually the hiring process is accomplished during some specified time period. The Director or responsible manager should engage new employees early and often to assure a good start and to build open and trusted relationships with already hired laboratory staff. The completion of the hiring process and time to reach full functional employment may take weeks or months depending on technical complexity and requirements.
- **Selection criteria:** Section Managers or supervisors within the laboratory must play the central role in selection of suitable new team members. At the time of hiring it is important that the first line of management communicate to the employees, expectations and all relevant administrative and related technical information. It is important to have well defined job descriptions before initiating the hiring process (see Appendix 3 for sample job description).

- **Socialization:** The laboratory working environment and culture, including any specific rituals, should be explained to all new employees early in the process. Introductions and facilitation of open lines of communication and socialization among new and senior members of the staff are also important.
- **Resources and strategic alignment**: Leadership must consider resources and strategic alignment of the organization in individual hiring, always taking a broad view and considering the vision for the future.
- **Recruitment process:** While there may not always be hiring actions underway, the process of recruitment never stops. When resources allow, good leaders often hire an exceptional individual as the opportunity arises, rather than waiting until there is a position to be filled.
- **Selection of the best:** The most effective way to attract well-qualified and highly motivated staff for the laboratory is to be seen in the community as a "Best Employer".
- **Eligibility criteria:** Acceptable qualification and credentials for positions will vary with departments and organizational missions. Hiring authorities must give due consideration to age and technical qualifications as approved by the local laws and registration bodies. Job eligibility in terms of minimum qualification for each job; competency, in terms of experience, technical knowledge and any specific requirements should be followed strictly.
- **Job Descriptions and Laboratory standards:** Each laboratory should have prepared clear and concise job descriptions (JDs) for each category of employee and follow diagnostic laboratory policies and practices according to relevant accreditation standards or otherwise. Local laboratory policies should be in line with the relevant accreditation standards.
- **Ethical Principles:** All hiring, and personnel actions should be based on merit, openness and accountability with appropriate documentation. Always give due consideration to Conflicts of Interest, real and perceived. Selection by a professionally competent person and selection of the best candidate should be the rule. At the time of hiring, the employer should provide details such as schedule of work, job summary/description, duties and responsibilities, working conditions, work location or locations, travel or transportation availabilities and relevant requirements.
- **Health and safety considerations:** Medical laboratory staff must give special consideration to health and safety. It is the responsibility of leadership to provide detailed information in this regard to all staff members. The information should be based on technical experience of the senior technical leaders, formal risk analysis and biological safety guidelines.
- **Selection process:** Key issues of consideration during the selection process include identification of capable selection team or committee, appropriate job application forms, resumes and applications from candidates, in-person and electronic interviews, testing and reference checking. It is advisable to plan an objective Applicant Scoring System when possible. It is also appropriate to consider 'in-house hires' or transfers; this practice can enhance employee satisfaction

broadly. Always keep in mind the previous experience and performance record of candidates. As stated, contingency planning for hiring can be effective to avoid any possibility of a critical vacancy in any section of the laboratory. Similarly, it is important to focus on succession planning. This involves taking steps to groom replacements for an anticipated vacancy well before the vacancy comes about.

- **Professional networking:** Active communication and interaction with other diagnostic laboratories within the healthcare system may lead to networking beneficial to the employee search and hiring process. Seeking advice from senior leaders or colleagues in the system or hiring professional recruiters is also being practiced. Networking is also a source of continuing education and staff development.

STAFF DEVELOPMENT AND CONTINUING PROFESSIONAL DEVELOPMENT

Staff development is a continuous process and must be a priority. Encourage and provide opportunities to the staff to participate in national and international continuing professional development programs whenever possible. Continuing professional education and development ensures that all employees are competent to meet the required professional goals. Staff continuing education instills confidence and job satisfaction that translates directly into a healthy organizational culture and a more effective laboratory. Further details of professional development are given in the chapter on Professional Development and Certification.

THE WORK-LIFE BALANCE

Visionary laboratory managers always endeavor to improve the work environment. The following leadership principles, when applied effectively and in the appropriate local context can contribute to a healthy working environment:

- Consideration of the needs and responsibilities of the 'whole person' is an important concept.
- Empowerment and autonomy for all sections of the diagnostic laboratory.
- A sense of fairness for all.
- Innovation in terms of changes to keep up with technology and challenges.
- Open communication within and between all sections of laboratory.
- Confident and constructive 360-degree feedback.
- Consideration and thoughtfulness to enhance personal and community spirit.
- Equal access for all regarding available benefits and resources.
- The concept of “Living the Values” based on integrity and healthy social norms and standards.
- Addressing the specific needs of each individual and balanced professional work load according to recommendations of national and international standards and in accordance with ethical human behavior.

EFFECTIVE COMMUNICATION WITH LABORATORY STAFF

Regular effective communication is a key, as all the staff members should feel that the laboratory leader or manger is providing necessary and relevant information. Leaders must communicate with all tiers of the organization fairly and consistently. Always practice active listening skills. Be open-minded and respect other's opinion. Seeking the advice

and perspective of technically skilled employees is not only valuable for future planning but results in their support of leadership and increased efficiency and effectiveness. Frequent interaction, particularly when leadership demonstrates interest in the detailed technical work of the staff, improves everyone's sense of responsibility and personal value to the organization. Leaders must choose their words; regular praise and reminders of common goals and organizational values are an effective means of communication. Be ready to listen to any criticism and accept the challenges with a positive attitude. If leaders demonstrate openness to listen and resolve problems equitably, it is more likely that an unhappy or disgruntled employee will come forward, seeking help in time of personal or family crisis. Good leaders want to hear the 'bad news' first; the 'good news' will take care of itself. A 360-degree evaluation and feedback can be an integral part of the communication mechanism in laboratory management. It allows each individual to look in detail at his performance and effectiveness as a coworker. It provides insight regarding the professional skills and behaviors desired in the medical laboratory to achieve the common goals. This technique can be utilized to assist each individual to understand his strengths and weaknesses and possible approaches to professional development. It is particularly important to both address and practice gender equality in communication and professional development of the staff.

GENDER EQUALITY AND CULTURAL CHALLENGES

The male to female ratio of medical laboratories may vary with culture of a given country or region. In some developing and underdeveloped countries, the percentage of female staff has been significantly low historically. With global changes and equitable education this ratio is changing in favor of female staffing. In medical laboratories it is important to achieve work-place equality by providing equal access to all the resources and opportunities and to assure a sense of security for all. Rewards, resources and opportunities should be based on professional competences and should be provided regardless of gender. Cultural and gender diversity plays a positive role but can be a challenge as well; it often requires education and leadership setting the example. Developing appropriate communication skills in a setting of diverse cultures is required of a laboratory leader. When making any decision about the organization of the medical laboratory due consideration must be given to personal values, practices, traditions or beliefs of different groups or individuals with special consideration towards age, race, ethnicity, religion and gender. Gender roles are not the only factors that stress organizations in this ever-changing new 'small world'.

CHANGE AND INNOVATION

Leadership's role in motivation and innovation cannot be under estimated in any diagnostic laboratory. Creativity and innovation in medical care are playing a vital role in present day patient management; the same is happening in laboratory medicine. Advances in healthcare require rapid changes and commensurate innovations in diagnostic tools and methods also. Leaders with a vision for innovation-driven goals can orient and motivate laboratory staff. Managers should encourage the staff to accept any positive change by facilitating the process. Identification of process bottlenecks and their resolution, wherever they occur within the organization, is important. One must engage the right person at the right time in the right direction. Developing habits of sharing new ideas, autonomy, collaboration and encouragement will help to overcome inertia and will

make any change pleasantly acceptable to all. Tapping new ideas from laboratory staff and providing resources for implementation will add to a positive working culture. Fanning the passions to create, finding the courage to face failure or any difficulty and convincing the bureaucratic systems above to understand the importance of diagnostic laboratories will make this process a success and enhance employee loyalty. Organizational ingredients that can truly energize the staff include teamwork, an attractive work environment, professional development opportunities, transparency and regular objective appraisal. These factors will also help in creating a collaborative and progressive environment in any diagnostic laboratory. Not only is communication important within the laboratory; communication to and from the laboratory within the entire healthcare system must be timely and accurate. This is another technical field, which has advanced rapidly in the past few decades (see Chapter 12).

COMMUNICATION AND INFORMATION TECHNOLOGIES

In any component of the healthcare system, diagnostic work-ups and physician-patient communication play a pivotal role. Patients and treating physicians rely on timely communication and interpretation of laboratory results. Laboratory informatics is essential for data collection and informing patients and health-care providers of laboratory and diagnostic test results. For this and other reasons, establishment of a comprehensive communication system and efficient IT department within the diagnostic laboratory are fundamental. The laboratory manager's understanding of and trust in the possible benefit of this significant investment is critical. The role of information technology is also important for improving patient safety through identification, communication, and reliable documentation. It is becoming important for diagnostic laboratories to choose a laboratory informatics solution that is comprehensive and has long-term utility. Such a system will also help in managing a laboratory remotely and in collaborating with other laboratories. Laboratory systems should be compatible across a nation or region for greatest efficiency and positive impact. Laboratory leaders often rely heavily on technical experts in establishing IT systems but should have at least a working understanding of the technologies. Excellence in electronic communication obviously contributes to quality performance and is a necessary part of a quality management system. Keeping pace with the new concepts and development in the field of artificial intelligence relevant to diagnostic will be essential at all levels.

QUALITY MANAGEMENT

As highlighted in the World Health Organization's (WHO) Handbook on Laboratory Quality Management Systems, achieving, maintaining and improving accuracy, timeliness and reliability are major challenges for health laboratories worldwide. Part of a leader's responsibility is to inspire and organize through establishment of a comprehensive quality management system.

The concept of Total Quality Management (TQM) and its implementation should be etched in the vision and goals of each component of diagnostic laboratory function. The leadership should sponsor a quality management system through shaping the culture, which is essential for implementation and continual improvement. Quality management is also important for medical laboratory certification and the accreditation process. All sections of the diagnostic laboratory should be encouraged to participate regularly in

internal and external quality programs as recommended by the local health authorities. While planning and budgeting may seem mundane or unimportant to a highly technically qualified individual, they are also an essential part of the greater laboratory structure and functions. The subject has been dealt with in detail in the chapters on quality management (see Chapters 19 and 20).

PLANNING AND BUDGETING

Most diagnostic laboratories have separate budgeting and planning departments, but the functions are combined in some labs. It is essential for the laboratory managers and leaders to understand and provide timely strategic advice to these departments. It is advisable to be conservative and careful about overly optimistic financial forecasts. In most instances, local governments or hospital systems provide allocated funds and set healthcare policy. It is best to develop the budgeting activity with a leadership team and always make use of available consultancy. The task of annual or emergent budgets should be allocated to those individuals from the laboratory staff that have insight regarding future planning and a sense of the diagnostic requirements in a particular situation. Always spend adequate time in planning and allocation of funds to various departments of the laboratory. Comprehensive documentation of the complete budgeting process is an important safeguard. Everyone involved in the process should understand the documentation. Diagnostic laboratory managers and leaders should be provided opportunities to obtain continuing education regarding budgeting and its principles.

LABORATORY SAFETY AND SECURITY

Unlike planning and budgeting, laboratory safety is everyone's business. The role of diagnostic laboratories is to provide optimal diagnostic support required for the management of patients and prevention of disease. At the same time each laboratory must provide a safe environment for its staff and manage facilities, equipment and procedures in a way necessary to protect the environment. In accordance with local authorities, diagnostic laboratories are required to ensure implementation of various policies and procedures to ensure safety at all levels. In recent years, laboratory leadership has also been asked to consider 'security' of laboratory pathogen cultures, reagents and equipment. Biological Security is now often usefully considered along with Biological Safety under the concept of “Risk Assessment”.

Leadership must adopt and ensure that all employees embrace a culture of safety. Principles of employee and patient safety and safe disposal practices for any possible biological or hazardous waste from the laboratory must become part of the culture. Leadership plays the vital role in generating awareness and priorities regarding safe and secure diagnostic laboratories. Regular safety training and workshops arranged for the laboratory staff should be an essential component of continuing professional development for all. Biological Safety and Biological Security must become part of the culture of today's laboratories. They are not a 'product' of the laboratory, but without them, the lab will likely not succeed in today's global environment. Leaders must set the tone by accepting overall responsibility and supporting rational and reasonable best safety practices and by supporting the safety staff within the laboratory who are directly responsible (see Section II for relevant information regarding laboratory safety).

THE POWER OF COMMUNITIES OF TRUST

As we stated in the beginning, teamwork is the key to a successful laboratory. Teams can only function at their optimal level when they become communities of trust. While individuals at all levels can build or tear down trusted relationships, laboratory directors and key management leaders have the greatest opportunity to make a difference in a positive way.

An enlightened and effective leader steers with vision and an emphasis on quality science, safety, education, responsibility, accountability, honesty, transparency and ethics. The result will be what Steven Covey calls a “high trust organization”, with increased value, accelerated growth, enhanced innovation, improved collaboration, stronger partnerships, better execution, and heightened loyalty. Such an organization is unstoppable.

BIBLIOGRAPHY

Balancing our Approach to the Insider Threat. Franz, D.R. and LeDuc, J.W. Biosecurity and Bioterrorism; Biodefense Strategy, Practice and Science. Vol 9, No. 3, 2011.

Barling, J., Slater, F., Kelloway E.K. Transformational leadership and emotional intelligence: an exploratory study. Leader Org Dev J. 2000;21(3):157-161.

Counts, J.M. Washington Clinical Laboratory Initiative: a vision for collaboration and strategic planning for an integrated laboratory system. Clin Leader Manag Rev. 2001;15:97-100.

Continuing Personal and Professional Development at UCL. Available at: www.ucl.ac.uk/hr/od/resources/continuing_prof_dev_guide.pd.

Gender Equality and Culture. Available at: http://www.unesco.org/new/en/culture/gender-and-culture/gender-equality-and-culture/

Guarner, J., Duncan, A., Nelson, A.M., Messele, I. Laboratory quality control for all can this be achieved? Am J Clin Path. 2012;138:639-641.

Leadership Vision. You Can't Be a Real Leader Who People Want to Follow without Vision. Ed. Susan, M.H. Updated October 12, 2016.

Safe management of wastes from health-care activities - World Health. Available at: www.who.int/injection_safety/toolbox/docs/en/waste_management.pdf.

The new science of building great team. By Alex, Harvard Business Review; April 2012.

World Health Organization Laboratory Quality Management System Handbook. (2011).

WHO | Health-care waste. Available at: www.who.int/mediacentre/factsheets/fs253/en.

The speed of trust: The one thing that changes everything, Covey, S.M.R. Simon and Schuster Company (2008).

Chapter 2

Best Laboratory Practices

Ayesha Junaid, Shifa College of Medicine; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory; Muhammad Tahir Khadim, Armed Forces Institute of Pathology, Rawalpindi

DEFINITION

Laboratory test results have an impact on people's lives. Clinical laboratory test results could identify a person as suffering from a certain medical disorder, despite he or she being completely asymptomatic and feeling fine. Forensic test reports can change an individual status from an innocent to criminal or vice versa and genetic testing can reveal susceptibility to a heritable disease. Such is the strength and influence of a laboratory test result; revealing the true picture of the tissue changes or body chemistry. All those steps which ensure that the laboratory tests are valid and accurate constitute best laboratory practices (BLP). This chapter discusses eleven key components of BLP.

BEST LABORATORY PRACTICES

1. Personnel

Personnel selection and task assignment are the most important jobs in laboratory management. The best equipment cannot produce quality work without a competent and conscientious technologist. After hiring an educated and experienced person, his/her performance level on all the tasks in the department should be documented. If the selected person is unable to perform any specific task/test in a section, bench work training before independent duty assignment for mutually agreed period must be mandated between the technologist and the supervisor.

All team members should be regularly trained to maintain their performance level. As new tasks /tests are added, continuing medical/professional education, training sessions and regular evaluation of practical performance of all team members must be ensured. When purchasing any new instrument/technologies, due consideration is to be given to include the training package through the manufacturer. The supervisor must update the proficiency grid of all the team members regularly.

2. SOP Writing

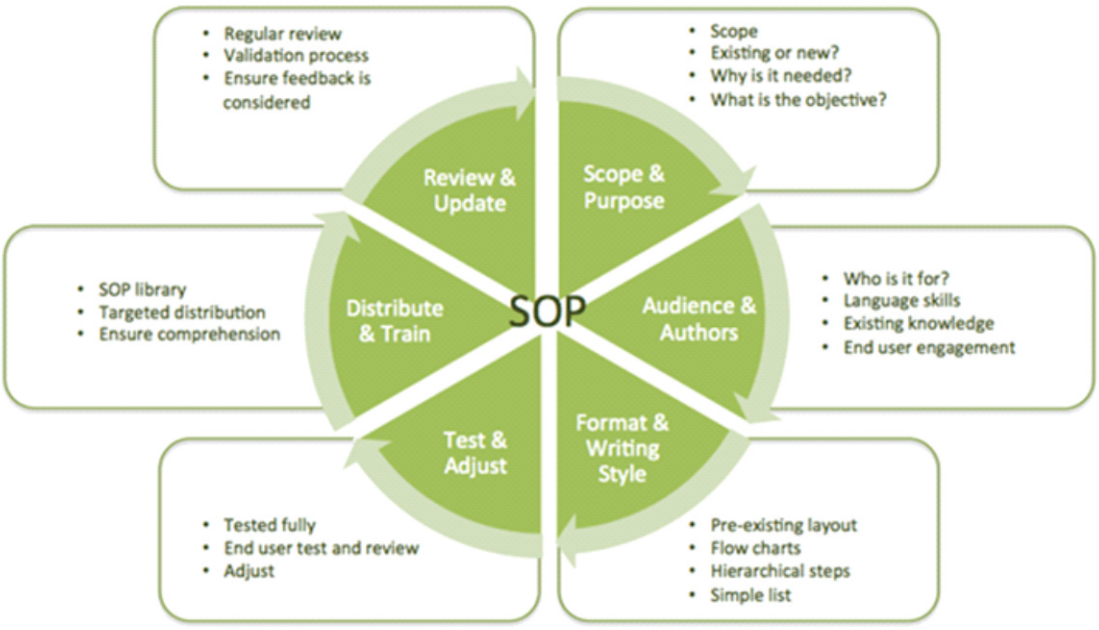


FIGURE 2-1: Key Elements in creating an SOP (Collaboris; www.collaboris.com)

Standard Operating Procedure

It is important to ensure that each standard operating procedures is relevant and useful for the laboratory personnel; however, it may differ slightly between laboratories. The following SOPs are essential for all clinical laboratories:

a. SOP for receiving the samples (central/departmental receiving)

This SOP is necessary for tracking samples and shipments as they come into the laboratory. The SOP may include information that need to be recorded, such as: time of receiving, person receiving, package/sample condition (container and quantity of samples, temperature of specimen), package/sample storage, and more.

b. SOP for accession

This is important for when a sample is being added into an inventory, information is being entered into a database, or the sample is being passed from one individual to another. Samples should be properly labeled and assigned to the correct team for testing.

c. SOP for the analytic part

All testing performed in a clinical laboratory should follow the predetermined SOP for each specific test. This ensures that all tests are being run in the same manner and helps to achieve consistent results. SOPs for tests should be written in a detailed and step-wise manner (See Chapter 10 for more information on preparing a laboratory procedure manual).

d. SOP of stat/ routine & panic reporting

Clinical testing is important for many medical procedures and prompt reporting of results can change the course of treatment, thereby saving lives. The prompt and

accurate reporting of clinical findings is necessary. A detailed SOP regarding the recording and reporting of test results will help to ensure that all test results are reported currently and efficiently. The SOP for reporting should include information regarding whom to report the results, how to handle panic values, and how to properly record test results. Since errors can occur with verbal dictation of results, read-back of any results and double checking of all values and units is very important.

e. SOP on post-analysis retention time of the sample

Given the clinical importance of some samples, laboratories may choose to store the sample for a certain period of time after completing testing. This may be beneficial for re-testing of samples, or for potential use of further testing in the future. In order to store samples after analysis has been completed, an SOP will help define how long the sample will be stored, where/how (type of container, temperature, location) and the sample date.

f. SOP for proper disposal of the samples

All materials should be disposed of according to the correct biohazard level. (See Chapter 11 on Laboratory Waste Management for necessary information regarding waste SOPs).

g. SOP for judicious use of resources

Using resources efficiently can save a clinical laboratory time and money. However, running batches of samples at once may increase the potential for error or mislabeling. An SOP defining how and when to run batch analysis on samples should help guide laboratory technicians. This SOP should clearly define the type and number of test samples that can be run in a batch, how to use control reagents efficiently and include guidance for the proper labeling and tracking of all samples so that the correct results are achieved.

3. Work Bench Assignment

When an instrument is used by only one staff member, usage time, calibration, maintenance and other issues are minimized. When the instrument is being used by multiple staff members, assigning these responsibilities to a primary and senior user, is the right practice. The responsible person should schedule usage time for other staff members, provide training and mentoring to new users, ensure that controls are run and followed according to the written policy. This person can also ensure that calibration logs and maintenance schedule are strictly adhered.

4. Instrument Calibration

Calibration is performed to ensure instruments' accuracy; demonstrates that the instruments read the correct value assigned to a standard substance. Calibration should be conducted at the time of installation and periodically as defined by the biomedical department or per manufacturers recommendation (e.g. after receiving new lot of controls, weekly or monthly calibrations depending on equipment usage). If re-calibration resolves a simple one-time error, then the instrument can be reused with documentation of the date and detail of problem in the instrument maintenance log. In all other situations where a known result is not received, the instrument engineer/backup service must be called.

5. Method Validation

Method verification is necessary to choose a method that produces an accurate result within an acceptable uncertainty that can be performed by multiple analysts. Individual laboratories will develop new method or modify existing methods to address specific test needs they encounter. Each time a new test is started or a new kit for an already in-use test is dispensed, an "in-house method validation" is a requisite. Every laboratory must be able to defend its chosen method as capable of offering accurate results, achieved through method validation (may already be in-use by multiple organizations and/or analysts for the same test). Successful validation requires that the results of multiple runs are all within an acceptable uncertainty value i.e., has a statistically acceptable margin of error. Method validation would involve use of control charts /use of Standard Reference Material (SRM) by different analysts in order to document the limit of uncertainty, accuracy & reproducibility. Research laboratories using the method for the first time should publish their method in the peer review journals in precise detail, so that systematic errors can be identified by following the same steps in another environment.

6. Control Charts

The control graphs enable a laboratory to track the results of a control material at the end of a specified time or after a specified number of tests. It indirectly provides a summary of the quality of the test run for the defined period of time. An acceptable control limit is defined for each parameter and deviations from the limit would indicate a visually measurable trend/outliner, which can be instantly identified. If the control charts show obvious drifts/out of limits readings, the reporting laboratory is mandated to notify the patient of potential erroneous results.

7. Proficiency Testing (Inter-laboratory Comparison)

Proficiency testing is the testing of unknown samples sent to a laboratory by regulatory/accrediting bodies to compare the results of participating laboratories. Proficiency testing (PT) refers to comparing the results of your laboratory with other laboratories using same instruments and methodology on samples provided by some external regulatory body.

For international accreditation, participation in PT 2-3 times a year is suggested. This exercise monitors the continuous laboratory performance; results reported by each laboratory are compared to the reference value for that analyte. The reference value can be determined by either taking mean of all reported results or by using one reference laboratory as the correct value and assigning acceptable range by ± one to two standard deviations (SD).

8. Duplicate Run

Duplicate runs during clinical testing can build confidence in results. For critical tests or the tests with border line/grey zones results, duplicate testing builds up the confidence in replicating data, help method reproducibility but cannot ensure accuracy. Duplicate testing can also be performed with reference material or with known values.

9. Documentation

A JOB NOT DOCUMENTED IS A JOB NOT DONE

All processes /activities need to be documented in an orderly and retrievable way. Documentation of method validation, proficiency testing, instrument calibration and test reports, all need to be archived for the possible physician's/patient's queries in case of panic and critical reports. Proper documentation is also a requirement by the regulatory bodies and additionally for legal matters.

In cases where the test results caused harm or near harm, documents can help to validate that the laboratory followed the standard methodology and thus can minimize or eliminate liability. In the absence of proper documentation, test result validity cannot be proven.

Documenting receipt of a critical sample by two identifiers by the technologist, would help inculcate ownership of a critical activity and would expedite the working on the test sample with individual responsibility.

10. Keep Original Data

"IF YOU CAN'T ACCESS A DOCUMENT, YOU HAVEN'T DOCUMENTED IT SUFFICIENTLY"

The use of electronic databases within laboratories is now standard. This has numerous advantages including less storage space and prompt retrieval. Dual servers or copying the analyzer's data to laboratory information system (LIS) should also be available for all the clinical reporting parameters.

In case the electronic database is not available, meticulous manual record of every laboratory activity is a must. Error/accident logs (electronic/manual) must also be saved and utilized for planning future preventive strategies. REMEMBER: The most important point about storing data is easy accessibility and data back-up.

ETHICS AND PROFESSIONALISM

Introduction

In laboratory practices, many situations involve thoughtful considerations that have important implications for all the stakeholders. The decisions in such situations entail knowledge of medical ethics or bioethics. It is truly understood that the main objective of ethics is to place the human at the heart of medical care with the notion 'do no harm'. It also delineates our conduct as it deals with what we should or should not do as a professional. It is a test of workers' morality and accountability as bioethics deals with various aspects of life and death. Constant changes in society and values further enhance the importance of ethical practices. Other factors making the need of ethics essential in laboratory practices include, social pressure for individual rights, patients' confidentiality, patient safety, individual and community rights, rapid progress in science and laboratory practice, role of healthcare providers and research laboratories in life and death. There is always a relationship between moral, ethics, accountability and law.

A profession can be defined as an occupation that regulates itself through systematic, required training and collegial discipline. Any profession has its base in

technical knowledge or specialized skills. The medical or scientific knowledge has a service rather than a profit orientation in its code of ethics, and the same applies to laboratory sciences as well.

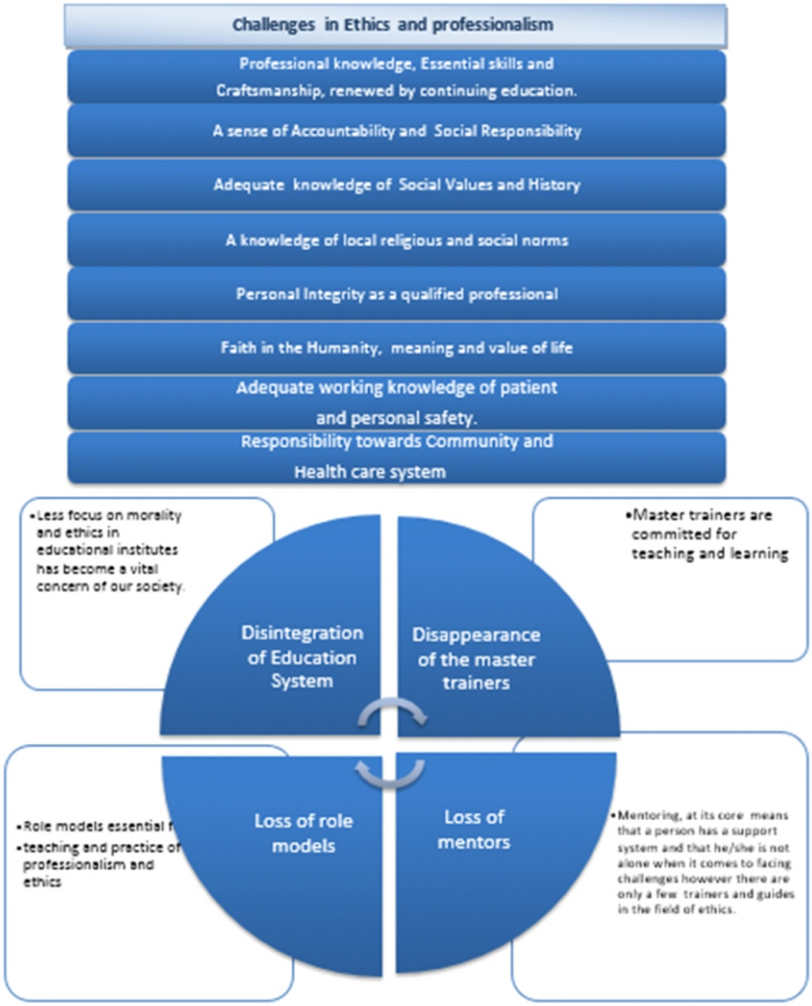
There are many definitions of professionalism; some define it as the skill, good judgment, and polite behavior that is expected from a person who is trained to do a specific job. Others define it as a specific conduct aims, or qualities that characterize or mark a profession or a professional person. Ethics and professionalism go hand in hand.

ESSENTIALS OF ETHICS AND PROFESSIONALISM

As defined by Royal College of Physicians UK "Professionalism is a set of values, behaviours, and relationships that underpin the trust the public has in doctors." The following can be considered as the basic essentials of ethics and professionalism:

1. Training is an intellectual process that involves knowledge. Practices after acquisition of appropriate training is compulsory for any profession.
2. In healthcare profession and laboratory practices, professional work success should be measured by more than financial return.
3. Professionalism should not be influenced by market economy or any other social diminishing factor in the society.

ESSENTIALS COMPONENTS OF PROFESSIONALISM



HOW TO LEARN PROFESSIONALISM?

Acquisition of a knowledge base:

A professional person is known for his/her specialized knowledge achieved through constant learning and practical application. Medical laboratory practices demand essential knowledge in order to practice successfully. This does not end here, professionals are constantly required to keep their knowledge up-to-date so that they can stay relevant and deliver expected standards of work.

Acquisition of skills:

Professionals should acquire set of skills that can help them achieve their goals. They need strong commitment to develop and improve their skills that can boost their performance and help them deliver in adverse situations as well.

Learning and understanding ethical standards, social roles and responsibilities:

Professionals should have clear understanding of their role and responsibility so that they can exhibit qualities such as integrity and honesty in their dealings. A professional thus never compromises values and will follow the set standards even if that means facing hardship and resistance in the process.

Accountability:

Concept of accountability is the single most important aspect of professionalism. A professional should always take responsibility for his/her decisions and actions, especially when a mistake is committed. This concept is strongly tied to integrity and honesty mentioned above.

Expert opinion to evidence-based practices:

The aim of a professional should be to provide the best care available through informed decision making. This requires extensive research to collect evidence and build expertise. This form of working promotes curiosity, compels a person to question their methods and thus ensures that actions are supported by strong evidence.

Self-interest to teamwork and shared responsibility:

Team building not only contributes towards motivation but also creates an environment of trust, thereby ensuring personal growth as well as more productivity. It improves understanding and cooperation, and this is reflected in the quality of work delivered.

PRINCIPLES OF PROFESSIONALISM IN HEALTHCARE PROFESSIONS

In today's world, the art of perfecting professionalism has become vital in every field, especially healthcare. There are three key tenets that dictate the principles of professionalism in medical practice; the first of which relates to the importance of patient welfare. This principle revolves around selflessness and dedication towards the needs of the patient. Only when that is assured can a rewarding relationship be struck with the patient. Mind, however, that any exogenous factors must not hinder this principle, for

example any socio-economic factors that may make alternatives more rewarding to the physician.

Social justice constitutes the second pillar. Dedication towards humanity must be the utmost goal, the healthcare profession needs to promote equitable distribution of healthcare resources, irrespective of any social, ethnic or financial background. This is only attainable if such distribution is actively pursued by all engaged in healthcare.

The final principle concerns patient autonomy. Without overriding any decision, the professional healthcare worker must respect any and every decision the patient deems best for him/herself. As long as such decisions fall within the acceptable dictum, the professionals like laboratory staff should always respect the patient's decision. That, however, does not discount in any way, the opinion that the physician is entitled to provide to the patient in all truth and honesty.

COMMITMENTS OF PROFESSIONALISM

There are certain commitments related to professionalism that complement the aforementioned three principles. The medical professionals to maintain the highest standards, as well as not to embark towards neglect or cause for concern must always uphold such commitments. These include:

Commitment to professional competence:

All professions especially healthcare providers must adhere to the standards set (as a minimum), or may even exceed those standards, but must not adhere to dealings that may tarnish the competence of the medical profession. The field of medicine demands a high level of competent commitment, since even a small error could possibly affect millions of lives. That is one risk nobody can afford to take.

Honesty with patient:

This aspect pretty much falls parallel to the principle of patient autonomy. We must, at all times, to best of our knowledge, provide an honest outlook to the patient and offer the various avenues towards successful treatment. Again, this however does not mean disempowering the patient's ability to make decisions for him/herself.

Patient confidentiality:

In a contemporary world where confidentiality has become the crux of all good relationships throughout all industries, the same is expected in the medical field. Everyone must commit to not hindering the implicit goodwill between the patient and him/herself by confiding the patient's information with third parties. Only in extreme circumstances where the patient has given full discretion to make the relevant information public is the physician allowed to deviate from this commitment.

Appropriate patient-doctor relationship:

Much of the ethics that must be observed by laboratory revolve around this crucial factor. For efficient and effective disease treatment, diagnosis and follow up, an appropriate patient-doctor relationship needs to be struck from the get-go. Without this crux, the foundation of the field of medicine would collapse. Therefore, it is no wonder that

medical students are taught the importance of observing the ethics necessary for establishing such a relationship from the beginning of their studies, where patients are not just treated as patients, but as fellow human beings with whom they must empathize and offer their full support.

Improving quality care and access to care:

The laboratory science requires continuous improvement; a desire should be present inside the staff that compels them to never be satisfied with a certain level of progress, and always strive for more. This is crucial to medical field as a whole, since without this commitment, new and improved ways to deal with typical diseases as well as inventing solutions to unheard diseases would not be possible. The health professionals must strive towards high quality standards.

Scientific knowledge:

Practical application requires specific scientific knowledge and expertise in order to deliver results. Individuals should thus have adequate knowledge in their field for efficient and effective performance.

Maintaining trust by managing conflict of interest:

Situations that give rise to conflict of interest should be identified and resolved immediately. First step should be to disclose if there is an apparent conflict of interest, this requires self-regulation and honesty at the part of the physician.

Professional responsibilities:

Taking responsibility for decisions and actions is a vital trait of a professional. It is the duty of the professional to obey the rules and regulations and put the interest of their patients ahead of their own self interests.

KEY ELEMENTS OF PROFESSIONALISM

As stated in Project Medical Professionalism 2002 (American Board of Internal Medicine 1995), the key element of professionalism in medical and allied sciences are:

- Altruism;
- Accountability;
- Duty towards healthcare;
- Professional values;
- Excellence in professional care;
- Integrity and respect for others.

Laboratory practices must aim at production of highly skilled technicians necessarily true professionals. All the practices must strike a balance between explicit teaching and experiential learning incorporating the values of professionalism.

FURTHER READINGS

Accreditation Council for Graduate Medical Education. 1999. ACGME Outcome Project enhancing residency education through outcomes assessment: General competencies. Available at: http://www.acgme.org/outcome/comp/compFull.asp

Adams, J., Schmidt, T., Sanders, A., Larkin, G.L., Knopp, R. Professionalism in emergency medicine: SAEM Ethics Committee, Society for Academic Emergency Medicine. Acad Emerg Med. 1998;5:1193-1199.

American Board of Internal Medicine. Committee on Evaluation of Clinical Competence. 1995. Project professionalism. Philadelphia: ABIM.

Arnold, L. Assessing professional behaviour: yesterday, today, and tomorrow. Acad Med. 2002;77:502-515.

Arnold, L., Stern, D.T. 2006. What is medical professionalism? In: Stern, D.T. Ed. Measuring medical professionalism. New York: Oxford University Press. pp 15-38.

Arora, S., Ashrafian, H., Davis, R., Athanasiou, T., Darzi, A., Sevdalis, N. Emotional intelligence in medicine: a systematic review through the context of the ACGME competencies. Med Educ. 2010;44:749-764.

BIBLIOGRAPHY

Good Clinical Laboratory Practice Standards. Final Version 3.0; 9 July 2013.

21 CFR § Part 11 College of American Pathologists Commission on Laboratory Accreditation, Accreditation Checklists, 2012.

HANDBOOK GOOD LABORATORY PRACTICE (GLP) Quality practices for regulated non-clinical research and development.

Chapter 3

Training, Certification and Continuing Education of Clinical Laboratory Personnel General principles

Muhammad Tahir Khadim, Armed Forces Institute of Pathology, Rawalpindi;
Maureen Sullivan, Minnesota Public Health Laboratory

"**Acquire knowledge and learn tranquility and dignity**".
Omar Ibn al-Khattab

CONTINUING PROFESSIONAL DEVELOPMENT

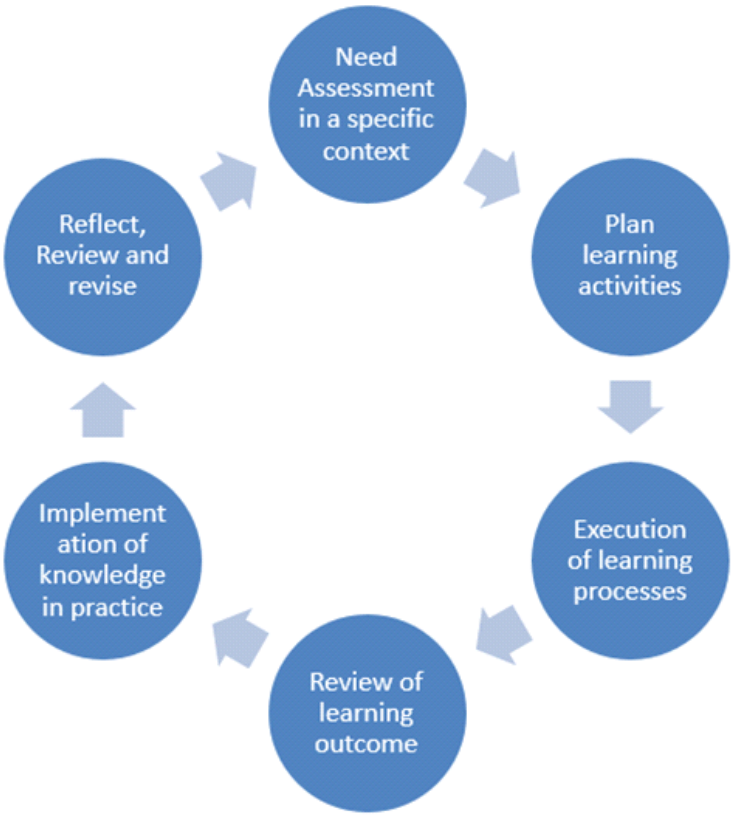
Introduction

Continuing Professional Development (CPD) as is commonly referred to is the process of tracking and documenting the skills, knowledge and experience that is gained formally or informally beyond initial training including professional knowledge, managerial skills, social and personal skills. When it precisely concerns medical doctors, it is called continuing medical education (CME); for nurses it is continuing nursing education (CNE).

The aim of implementing CPD is to encourage all concerned stakeholders including doctors, pathologists, paramedics, and medical laboratory technologist (MLT) to commit to a life-long process of continuing professional learning through education and training. CPD enhances professional strength by keeping pace with rapid advances in biomedical technology in term of knowledge, skills and practical experience. It will also ensure that workers are competent in providing quality service in a multi-disciplinary healthcare environment.

CPD Cycle

The sequence of whole process depends upon may aspects of healthcare system and level of diagnostic laboratory. The typical cycle may evolve through following steps:



Purpose and Goals of CPD

As the world rapidly advances, a professional may face different challenges. A CPD program can ensure that the professional competencies are maintained throughout the career. The main goal of any CPD program is to keep laboratory staff updated to meet the needs of patients, the health service, and their own professional development. This is warranted because any academic knowledge has a shelf life. It also requires a documented activity to ensure translation of learning into action.

Over the time, CPD records achievements and professional documents which can be reviewed to see what has been accomplished as yet and lay out future objectives and goals. While doing this, the organization realizes the gap between its skills and capabilities which guides future needs for development. When an organization adopts a CPD program the purpose is to target people who are already qualified in their professional studies but can further enhance their skills and capabilities through continuing education. The importance of this can be judged by Albert Einstein's famous quote, “Education is not the learning of facts, but the training of the mind to think.”

CPD Essentials

CDP is a continuous process as it starts after the initial attainment of professional qualifications and is constantly sustained throughout one's career. It is associated to every profession. Medical science is one of the most important due to the rapid changes in the activities related to the practice of biomedical sciences. Since the professional practice is constantly evolving, personal knowledge, skills and behaviors must grow in keeping with current best practice. Learning new skills and keeping up pace with new practices must be essential for promotions. The potential for moving up the career ladder can help motivate employees to embrace a CDP program. This becomes the sole responsibility of the laboratory organization or leadership to implement and guide the employees towards adaptation of CPD which is successful only once it has been made part of the organizational culture. It is advisable to clearly define some incentives for the success of CPD program.

CPD does not necessarily involve any examinations, it is just a part of normal routine that involves internal and external peer discussions and reviews. At times this may be essential for the recertification process as after an organization has been accredited the best way to maintain the standard is CPD. Though these do not require large amounts of funds, if the need arises they can be financed through the laboratory budget.

CPD Activities

CPD does not involve any specific activities that need to be conducted in a linear sequence rather it involves simultaneous activities that are to be conducted along with the routine work of the professionals. These can include diverse range of activities suitable for the objectives and goals of development outlines. Some common examples of activities that can aid in CPD include:

- Academic activities like short courses, lectures, scholarly articles, e-learning).
- Workshops; a major breakthrough technique to brush up the knowledge.
- Research and publications.
- Conferences, symposia, seminars; attending, speaking, posters, etc.
- Training and Mentoring.
- Promoting professional values.
- Networking with colleagues for peer reviews.

Scope of CPD Programs

CPD programs and activities must be organized by accredited program providers or have been accredited by the CPD accreditation sub-committee of the concerned board or authority. They should be:

1. Designed to be cost effective, with the flexibility of providing a wide variety of choice to meet professional needs and further career development.
2. Incorporated with a quality assurance mechanism and a clear set of objectives.
3. Able to enhance participants' proficiency in the biomedical sciences profession in terms of specialty development, research, laboratory management, good laboratory practice, etc.
4. Able to impart to the participants, up-to-date knowledge and skills relevant to biomedical sciences through suitable training infrastructure.

Proposed CPD Points for Accredited Programmes / Activities

These can be modified according to the policy of accreditation institute or organization.

Activity Category	Maximum CPD Credit points allowed to be earned from the category per cycle	CPD Program / Activity	CPD Credit point
Attending CPD Activities	No maximum credit point for this category	Being an attendee in an accredited CPD Program / activity	1 Credit point per hour 6 credit points maximum per day and 12 credit points maximum per single program
Public Presentation and Publication	5 CPD Credit points per cycle	Being a chair, speaker, presenter, panelist, and teacher/ trainer in an accredited CPD programme / activity	2 Credit points per hour or activity (whichever is greater)
		Giving a poster / abstract presentation	1 Credit point per presentation
		Being a sole author / first author / correspondence author of paper	3 Credit points per article
		Being a co-author of papers	1.5 Credit points per article
		Being a reviewer / editor of scientific publication	1 Credit point per publication
		Being an author / editor of a book relevant of biomedical sciences	Credit points to be awarded on individual assessment
		Being an author of articles in a newsletter	Credit points to be awarded on individual assessment
		Being an examiner / clinical assessor / supervisor of a project of a project or dissertation	Credit points to be awarded on individual assessment
		Being a technical assessor in accrediting medical laboratories	1 Credit point per hour
Self-Study	3CPD credit points per cycle	Reading journals or educational materials form quality assurance programme	1 Credit point per year
		Engaging in self-study with assessment	Credit points to be awarded on individual assessment

Note: Depending on the relevancy of the CPD activities, the CPD credit points assigned may be multiplied by a relevancy factor ranging from 0 to 1 (0 signifies no relatedness, 0.5 signifies partial relatedness and 1 signifies total relatedness). Therefore, the actual CPD credit points earned from participating in a particular CPD program / activity can be calculated by using the formula:

CDP Credit Points = Weighting x Relevancy

Where Weighting = the CPD credit points preliminarily assigned to a specific CPD program/activity e.g. an attendee of a 3-hour seminar will get 3 credit points (1 credit points / hour x 3 hours); and Relevancy = the degree of significance that the particular CPD program / activity can enhance participants' proficiency in the profession in terms of specialty development, research, laboratory management, good laboratory practices, etc.

Online Options

With the recent advances in technology, a huge number of online training options are available. A professional can get advanced training while being at the place of duty or home, by the best experts in the field. It is very cost effective (at times free of cost options are also available); and no travelling or absence from the place of duty involved. There are reliable and authentic sites which can be explored.

Some of these courses are sponsored by the well reputed universities and institutes all around the globe like Harvard, John Hopkins, Stanford, MIT, UC San Diego, Imperial College London, and so on. These courses of short duration usually 2-3 months. They also provide university certified certificates at different rates.

The concept of massive **open online course (MOOC)** has gained momentum all around the world which has various application including interactive sessions to recorded videos.

Some of the examples are:

edX	https://www.edx.org/
Coursera	https://www.coursera.org/
Others include well established institutes like:	
	Centers for Disease Control & Prevention (CDC) https://tceols.cdc.gov/
	Texas A&M Engineering Extension Service (TEEX) https://teex.org/
	Occupational Safety and Health Administration (OSHA) https://www.osha.gov/dte/outreach/training_providers.html
	Online options from Royal Colleges UK, other medical institutes, etc.

BIBLIOGRAPHY

Gelmon, S.B. Can educational accreditation drive interdisciplinary learning in the health professions? Jt Comm J Qual Improv. 1996 Mar;22(3):213-22.

Headrick, L.A., Knapp, M., Neuhauser, D., Gelmon, S., Norman, L., Quinn, D., Baker, R. Working from upstream to improve health care: the IHI interdisciplinary professional education collaborative. Jt Comm J Qual Improv.1996 Mar;22(3):149-64.

Kirkpatrick, D. Great ideas revisited. Training & Development. 1996;50:54-9.

Pakistan Medical & Dental Council. Guidelines for CME. Available at: https://umdc.tuf.edu.pk/admin/PDF/PMDC%20guidelines%20for%20CME.pdf.

O'Brien, M.A.T., Freemantle, N., et al. Impact of formal Continuing Medical Education. Do conferences, workshops, rounds, and other traditional continuing education activities change physician behavior or health care outcomes? JAMA. 1999;282(9):867-874.

Smith, D.P., Rogers, G., Dreyfus, A., Glasser, J., Rabson, B.G., Derbyshire, L. Balancing accountability and improvement: a case study from Massachusetts. Jt Comm J Qual Improv. 2000;26(5):299-312.

Smith, J.E., Fisher, D.L., Endorf-Olson, J.J. Integrating patient satisfaction into performance measurement to meet improvement challenges. Jt Comm J Qual Improv. 2000;26(5):277-86.

Chapter 4

Laboratory Design Guidelines

Uzma Bashir Aamir, National Institute of Health, Islamabad;
David Franz, U.S. Army Retired

The design and construction of a clinical laboratory must ensure provision of a productive working environment for laboratory users as well as compliance with the health and safety requirements according to national and international standards. Safety is an important parameter in lab design; lab planners must work with architects, engineers, and the end-user researchers. As multiple factors impact a laboratory's design, it is crucial that all stakeholders – from scientists, environmental health and safety staff, and facilities managers to architects, engineers, and construction managers – work together to ensure the plan will support health and safety, and ultimately increase productivity.

LABORATORY COMMISSIONING AND COMMISSIONING AGENTS

'**Commissioning**' can be defined as the process to document and validate that quality standards are met during construction of a laboratory facility. This ensures that the various systems for the laboratory building have been properly planned, designed/installed and tested to operate and perform in conformity with the intended design.

During commissioning, even though there is focus on the engineering control components compliance, the process covers the entire building's operational capacity. This work is generally undertaken by a Commissioning Agent/Engineering Firm, that has the necessary knowledge and experience in building design and equipment operation and maintenance. Commissioning can furnish information on prospective deficits that may impact different aspects of building operation such as energy efficiency, environmental conditions, building operation and maintenance, equipment function and worker comfort. When a laboratory building is commissioned, the assessment does not usually include applicable biosafety guidelines. The commissioning agents are responsible to ensure that the facility's maintenance personnel are appropriately trained in operation and upkeep of the installed equipment. However, formal commissioning of laboratory facilities is a relatively new concept in Pakistan. An effective laboratory design can impact health, safety, and productivity in the following ways:

1. Fulfil User Requirements

To design a lab that supports both safety and productivity, the design team must start by determining specifications based on:

- Intended use of the laboratory including what materials or processes will be used.
- Number of people expected to work in the laboratory facility.
- Space requirements for the various operations to be conducted therein.

These considerations ensure that everything included in the design will serve a purpose in supporting lab users' productivity. When the design is successfully implemented, workers will have the equipment and materials they need to carry out their tasks safely and efficiently. Therefore, a fundamental starting point for safe and efficient lab design is a series of discussions with the end-user regarding the mission and proposed function of the lab. This includes discussion on a stepwise series of processes that define the 'workflow' in the laboratory, so that appropriate design requirements may be included at each step.

In addition, consideration must be given to requirements of persons with special needs (physical disability, variable height or pregnancy etc.).



Figure 4-1. Laboratory Workflow (Adapted from WHO Laboratory Quality Management System: Handbook)

2. Reduction in Accident Risks

Proper lab design cannot remove all hazards because many accidents are perpetuated by human error, but inappropriate design may increase the probability of negative incidents. Hazards in the laboratory can be wide ranging from fires to falls, ocular damage, sharps penetration of the skin, spills and beyond, all of which can harm lab users and shut down or delay work. A laboratory designed for safety makes these accidents less likely. When users have adequate workspaces and aisles available, they are less likely to collide as they work; fires can be contained quickly using sprinkler systems. Chemical spills and other hazards can be managed quickly, and efficiently, particularly when appropriate warning systems, cleaning and response materials are available.

3. A Laboratory Layout Adequate for Activities

The layout of a well-designed laboratory includes correct equipment installation,

dedicated work spaces and appropriate storage areas. Proper design helps ensure adequate space availability and organization; for example, potentially hazardous materials and equipment can be positioned in areas away from heavy traffic flow and ventilation sources to avoid disruptive airflows. Proper lab layout also ensures that the ergonomics of the workspace do not impede workflow. This means that the lab is designed in a way that provides everyone ample workspaces and allows efficient execution of work processes by the workers/researchers in the correct order. This is especially critical in some lab types, such as clinical, Quality Assurance/Quality Control (QA/QC), or commercial labs, where lab users are more likely to move from process to process in precise sequences.

4. Emergency Preparedness

When designing a lab, it is crucial to include vital safety features, such as biosafety requisites, fire protection and detection systems, and emergency showers and eye wash stations. When the end-users understand that these features are easily available and are trained in their use, they can focus on performing their work/research with a greater assurance of security for their health and safety. In addition, labs should have accessible and well-marked exits to be used in case of any emergency or accident.

The laboratory should have adequate ventilation system to control the temperature and keep the atmosphere comfortable, especially as research shows that optimal workplace temperatures can increase productivity. When hazardous materials are being used, ventilation systems should be more advanced and may require features such as chemical fume hoods or Class II biosafety cabinets to control potential exposure and capture contaminants in laboratory air.

5. Adaptability for Future Needs

It is important to get a sense of how laboratory functions may change in the future; hence a design with some flexibility built in may include features that lab users might not need immediately, but could benefit from later; examples include more and/or moveable workbenches or advanced ventilation for work with chemicals or infectious materials.

As the scope of activities for laboratories is diverse, so are their design requirements; therefore, a detailed assessment is mandated prior to initiating laboratory design: procedures to be conducted, the quantities, types and frequencies of bio-hazardous materials and agents involved, information on the staff capacity and their work environment requirements.

THE CONCEPT OF LABORATORY CONTAINMENT

Classification of organisms according to risk groups---ranging from low individual and community risk up to high individual as well as community risk---does not fully explain how biological hazards will actually be handled in the laboratory setting. For example, the risk group system alone does not factor in the impact of the various procedures used for manipulation of a particular microorganism in the laboratory. Containment levels are therefore assigned to describe the minimum standards required for handling the organism(s) safely in the laboratory setting. In addition to the inherent characteristics of each organism, the containment system must also consider the engineering, operational,

technical and physical requirements for manipulating a particular pathogen. There are four containment levels (BSL-1 to 4) currently defined based on biosafety requirements that can serve as a guide to designing the appropriate laboratory setting. Detailed information regarding biocontainment laboratories can be found in the WHO Laboratory Biosafety Manual, and Biosafety in Microbiological and Biomedical Laboratories (BMBL) Handbook.

Biosafety Level 1 (BSL-1)

This refers to the basic laboratory, which is expected to handle agents that require biosafety level 1. It does not have any particular design requirements beyond those appropriate for a well-designed and functional basic laboratory. For example, there is no requirement for Biological safety cabinets (BSCs) at this containment level. An open bench top can be used for lab work, and containment is ensured by using practices that are generally recommended in a basic microbiology laboratory.

Biosafety Level 2 (BSL-2)

This refers to the laboratory, which is expected to handle agents that require biosafety level 2 containment. The main exposure hazards associated with BSL-2 organisms involve ingestion, inoculation and contact with mucous membrane. The infectious agents that require BSL-2 facilities generally do not transmit through the airborne route, however precautions must be taken to prevent or minimize the generation of aerosols or splashes. In addition, this laboratory facility must be designed to accommodate primary containment devices including BSCs and centrifuges with sealed rotors etc. and use of appropriate personal protective equipment (gloves, laboratory coats, masks, protective eyewear). Availability of hand washing sinks and decontamination equipment such as autoclaves must be ensured to minimize environmental contamination.

Biosafety Level-3 (BSL-3)

This refers to the laboratory, which is expected to handle agents that require biosafety level 3 containment. These agents are transmissible through the airborne route, generally require a low infectious dose to manifest disease and can result in serious or life-threatening disease. The emphasis in a BSL-3 facility is on availability of additional primary and secondary barriers to contain infectious agent release into the laboratory and the surrounding environment/community. Strict control of access to the laboratory, HEPA filtration of exhausted laboratory air and mandatory use of respiratory protection are additional features that are added at BSL-3 to prevent transmission and spread. There may be requirements for immunization of personnel working in the BSL-3 laboratory.

Biosafety Level-4 (BSL-4)

This is the maximum biosafety level available and is appropriate only for facilities that handle microorganisms classified as requiring biosafety level 4 such as Ebola virus, Marburg virus, Crimean-Congo hemorrhagic fever and Lassa virus. These agents have the documented propensity for transmission by aerosol route, generally have a low infectious dose and often result in very serious and fatal clinical outcomes with generally no treatment or vaccine available.

This laboratory level mandates requirements for high containment with a structurally and functionally independent unit, preferably located separately from other research activities. BSL-4 emphasizes maximum containment of the infectious agent by complete sealing of the facility perimeter with confirmation by pressure decay testing; isolation of the researcher from the pathogen through use of a positive pressure suit or containment of the pathogen in a Class III BSC; and ensuring decontamination of air and other effluents within the laboratory facility.

However, it must be emphasized that most clinical laboratory settings including public health labs are assigned as containment levels 1 and/or 2.

BASIC PRINCIPLES IN CLINICAL LABORATORY DESIGN

There are certain basic principles to laboratory design, which can guide the end-users based on their requirements and plans for the facility.

Standard/Generic Labs

For those planning to design and construct a new laboratory, standard/generic plans are available. These plans often include calculations and information regarding the basic engineering services and casework that can be performed within the space. Design and installation of generic lab units is a practical alternative when information on the exact utilization of the space or nature of service or research to be conducted is either unclear or unavailable. A laboratory designed on a standard plan would also make sense from an administrative standpoint, as every research group or team receives the same basic facilities. However, standard or generic labs must have some in-built flexibility so that they are amenable to changes in casework or engineering services or installation of new /additional equipment. An excellent option in this regard is use of modular workspace in newly designed labs, that can be moved anywhere with the exception of sinks and fixed fume hoods that have to be connected to plumbing and air vents respectively. This allows for greater laboratory flexibility.

'Open' and 'Closed' Labs

The concept of creating "open" labs is increasingly being employed particularly in many research institutions in order to support diverse types of team-based work. In direct contrast to the previous concept of "closed" labs, which cater to the requirements of the individual research investigators, open labs are designed so that laboratory space, equipment, bench space, and even support staff are shared by various researchers, thereby helping to reduce the cost of research. The organization and resulting interdependence of the open laboratory not only fosters coordination and communication among scientists, but also ensures that the laboratory facility is easily adaptable for future requirements.

The 'open' laboratory design concept can be advanced by use of movable partitions thereby permitting dedicated workspaces as well as allowing people to see one another. It is important that if required, the architectural and engineering designs are incorporated into multiple floor plans, which may be modified based on the research teams' needs. Consequently, two or more open labs can be located on a single floor, thereby enabling multiple teams to focus on separate research analysis aspects of related projects.

Despite the positive attributes of open lab design, 'closed' labs are still required for certain types of research or for housing highly specialized equipment. Examples include tissue culture labs, electron microscopy, polymerase-chain reaction (PCR) and nuclear magnetic resonance (NMR), and darkrooms, which require equipment or activities that must be accommodated in dedicated areas.

Wet and Dry Labs

In general, clinical and research facilities have both wet labs and dry labs. A significant amount of bench work and handling of infectious materials is carried out in wet labs which typically have sinks, piped gas/vacuum sources along with fume hoods and chemical resistant countertops with fixed casework and 100% outside ventilation source. On the other hand, dry lab construction is generally very similar to office structure with air recirculation; these labs are usually computer intensive and therefore require significant wiring with data and electrical circuits, special resistant countertops and mobile casework. Dry labs require substantial air conditioning or cooling as a considerable amount of heat is generated by the equipment.

KEY ELEMENTS OF LABORATORY LAYOUT/DESIGN PLANNING

In order to adapt to diverse laboratory requirements such as routine diagnostic services and research projects, the key elements of laboratory layout must be ensured through:

- Flexible engineering systems and casework that allow alterations in spaces to meet the needs of various teams.
- Office and write-up (dry) areas designed as places where people can work in teams.
- Fewer or no spaces that are identified with a particular department.

Clear interior glazing to allow people to see one another.

RECOMMENDATIONS FOR LABORATORY CONSTRUCTION/ RENOVATION MATERIALS

Description	Unsuitable materials/options	Recommended/ Suitable
Walls/Ceiling	Friable wall/ ceiling tile or paints	Well sealed junctions with ceiling and floor, Paint/materials should be capable of withstanding washing with strong detergents and disinfectants
Doors	Narrow	Wider/higher size (up to 48 inches width), recessed, with outward swing; Vision panels recommended BSL-2 laboratories should have self-closing doors with locks
Windows	Open	Insect netting and closable windows
Floor	Carpeting, wood or small tiles, slippery, multiple joining areas	Non-absorbent, skid-proof, resistant to wear, and resistant to the adverse effects of acids, solvents and detergents
Work surfaces (e.g. bench tops and counters)	Porous materials such as laminate, wood tiles etc.	Impervious materials; composite stone (granite may be a local option), stainless steel
Sinks	Conventional Taps	Must be available for handwashing; elbow or sensor operated
Gas & Plumbing inlets/outlets	Connected with other plumbing,	Should be completely sealed Lab waste water lines should be separate from domestic sewage, back-flow prevention (anti-siphon) devices. Main shut off should be separate
Electrical	Extension cords and un-grounded receptacles	Earthed/grounded connections Maximize number of separate circuits to avoid overload Well-marked breaker boxes Emergency/back-up power available Emergency shut off switch outside lab

EQUIPMENT ZONES

It generally takes significant effort to plan, design and build a proper lab facility. Once the lab is operationalized, any emerging needs such as increase in workload, personnel and research requirements must be considered ahead of time. The designation of specific equipment areas or zones that can accommodate modifications easily is a cost-effective design option that will provide a large degree of flexibility. A good rule of thumb for a generic lab is 50–70% allocation for casework initially, preferably located along the outside walls, with islands/areas in the middle demarcated for large equipment as equipment zones. As a general recommendation, approximately 25% of the space in most labs is allocated for equipment zones. This in turn will provide adequate space to change placement of cabinetry/casework and equipment as well as make additions of new casework and/or equipment as necessary. Furthermore, it may also be helpful to locate 3 - 6 ft. areas for equipment close to the outer walls in order to accommodate gas cylinders etc. near incubators, fume hoods and freezers.

LABORATORY FURNITURE REQUIREMENTS

Laboratory work surfaces and furniture including workbench, desks, chairs and stools must be impermeable in order to allow prompt and efficient clean up and decontamination procedures in the event of a spill or accidental contamination. For instance, laboratory stools can be covered in plastic or vinyl finish instead of fabric or cloth. This principle must be applied strictly to all laboratories using hazardous chemicals, biohazards, or nuclear substances.

MOBILE CASEWORK/CABINETS

As more technologies become available and instrumentation automated, laboratories must have capacity to assimilate any additional equipment by provision of movable/flexible casework such as the use of affordable storage cabinets that can help maximize storage space, in comparison to multiple base cabinets. Use of mobile carts that are able to support heavy weight can serve as very suitable equipment storage units, as well as computer workstations. When there is sharing of instrumentation between labs, instrument cart assemblies provide an excellent mobile solution. From a practical standpoint, electrical ports at multiple locations and provision for wire management must be part of the casework design.

Similarly, mobile base cabinets that incorporate multiple drawer and door configurations can be used as required. Another option is the use of mobile write-up stations which can be moved in or out of the lab based on requirement for seated space for data entry or collection. Ideally, write-up desks should to be at least four feet wide to allow for knee space and hardware under the countertop. Ports and outlets should be located to accommodate multiple furniture layouts.

LABORATORY STORAGE SPACE

Use of overhead cabinets can provide additional laboratory storage space. Alternatively, or additionally, use of adjustable shelves instead of cabinets can add flexibility, allowing the lab staff to use the required number of shelves adjusting height and spacing as necessary. When further equipment adjustments are required on the bench,

shelves can be removed to allow additional space as necessary. As a general recommendation, the bottom shelf should be positioned 19-20 inches above the bench top and should stop at least 18 inches below the ceiling so that appropriate coverage is available by the sprinkler system. Some special recommendations include:

Shelving and edge guards: When open laboratory shelves are being used for storage of chemicals or any other hazardous materials, they should have edge guards with height between 12.7 mm to 19 mm (½ to ¾ inches).

Flammable liquid storage: Use of appropriate cabinets that are recommended/ approved for storage of flammable and combustible liquids is mandatory.

Corrosive liquid storage: Primarily, acids and bases should be stored separately and for this purpose, use of corrosion resistant-storage cabinet is recommended.

Compressed gases: Compressed gas cylinders in the laboratory present a hazard and must be secured by ensuring their attachment to a secure structure, typically a solid wall, by using non-flammable materials such as metal chains.

FLEXIBLE ENGINEERING SYSTEMS

Engineering services in the laboratory should be flexible and must ideally include availability of important utilities and facilities such as uninterrupted power, water, internet, gas/vacuum ports and supply and exhaust air sources. The ports for connection /disconnection of these supplies must be easily accessible whether located on walls or the ceiling in order to permit rapid and reliable equipment hook up.

When a new laboratory facility is being planned, the design should incorporate the following essential components:

- Provision of appropriate duct work where required to allow fume hoods or biological safety cabinets to be added or removed.
- Access to controls for maintenance outside the lab.
- Rapidly accessible service shutoff valves, located in a clearly labelled box on the wall or on the roof close to the laboratory entrance.
- Clearly labelled pipes, valves, and clean-outs identifying the contents, pressure, and temperature etc.

Lastly, the engineering support systems should ideally be designed to have at least 25% expansion capacity in anticipation of future laboratory needs. An example is future allowance for additional space in corridors, ceilings, and vertical vents for heating, ventilation, and air conditioning (HVAC), and plumbing needs.

LABORATORY VENTILATION

The following general principles apply to most BSL-1 and BSL-2 facilities particularly the latter:

- Window design must be integrated with the HVAC system to ensure that there

is no condensation, wetting and/or frost build-up.

- The laboratory air handling systems should provide inward directional airflow; non-recirculated air should be delivered to level 2 laboratories (this is not applicable to re-circulated air through equipment such as biological safety cabinets).
- Under routine operations, there should be a minimum of 10 air changes per hour.
- The HVAC air distribution must be designed to decrease dead air spaces within the laboratory; location of supply and exhaust diffusers must ensure convection patterns so that airflow is directed away from lab entrance.
- Laboratory containment structures (or facilities), including doors and windows, must be kept closed in order to provide required containment of air systems

SPECIFIC VENTILATION EQUIPMENT

Fume Hoods

Fume hoods are safety devices that are meant to protect personnel from chemicals with long-term exposure hazards. They are not suitable for protection from substances that may cause significant health consequences even on short-term exposure or contact. There are two basic configurations of fume hood that may be available in different sizes. One type is the bench top hood, which is typically placed on the laboratory bench while floor-mounted hoods, also called walk-in hoods, are positioned on the floor.

A fume hood commonly draws room air at approximately 100 feet per minute (fpm) at the sash opening, which is equivalent to nearly 1 mile per hour. Some important practices to eliminate the effect of competing airflows such as from the room air currents on the functioning of fume hoods include:

- Use and placement of supply diffusers to minimize competing airflows below 30% of the face velocity. For example, for a 100 fpm face velocity, the room air currents must not be over 30 fpm. Sufficient free space must therefore be ensured around the fume hood for this purpose.
- The fume hoods should be placed away from main walkways in the lab. Individuals generally walk at a speed of 2 to 3 miles per hour, which may create a “wake” that can potentially draw air out of a fume hood.
- The fume hoods should be located away from the laboratory doors because laboratories normally operate at a lower pressure than hallways. When the laboratory door is open, air is drawn into the laboratory, which can potentially disrupt the fume hood operation.

Fume hoods must conform to the local, national or international standards. For example, in the US, all new laboratory fume hoods conform to the CSA Standard Z316.5-04 (Fume Hoods and Associated Exhaust Systems). Existing fume hoods undergoing upgrades or renovations should also be compliant with the requirements of CSA Standard Z316.5-04. All fume hoods must be equipped with audible as well as visual alarms for warning when the face velocity drops below the recommended set point. All fume hoods should be tested regularly, according to manufacturer recommendations.

Laminar Flow Hoods

A laminar flow hood or cabinet is essentially an enclosed bench specially designed for provision of aseptic work area. Laminar flow hoods protect the lab bench working environment from dust and other airborne contaminants by maintaining a constant, unidirectional flow of HEPA-filtered air over the work area. These hoods are available in both horizontal and vertical configurations.

Biological Safety Cabinets

Controlling laboratory airflow as well as aerosol spread is a major aspect of protection and containment in clinical laboratories dealing with biohazards. Primary containment aims at protecting the worker and limiting or preventing contamination of the lab (and therefore the risk of exporting contamination outside the lab). Biosafety cabinets (BSCs) are one of the most common primary containment devices in biological research and diagnostic labs. Class II BSCs require regular attention as it is not unusual to find poor design, incorrect installation or irregular maintenance and certification in many part of the world (Whistler T. et al., Applied Biosafety, JABSA 2016, 21, 121-127).

The main personal and environmental protection features in Class II BSC include:

- A sensitive air barrier at the level of the front grill.
- HEPA filtration of exhaust air.
- Product protection (thanks to the HEPA-filtered laminar air flow).

Some of the limitations of this BSC class include:

- No protection against hazardous volatile substances (HEPA filtration does not provide protection).
- Sensitivity to air movement within and outside the cabinet.
- Sophisticated equipment requiring specific practices and maintenance.
- Relatively weak and “fragile” (non-robust) personnel protection.

High testing and maintenance costs.



Adapted from a biosafety cabinet workshop conducted by Pakistan Biological Safety Association (September 6-7 2018 in NARC, Islamabad)

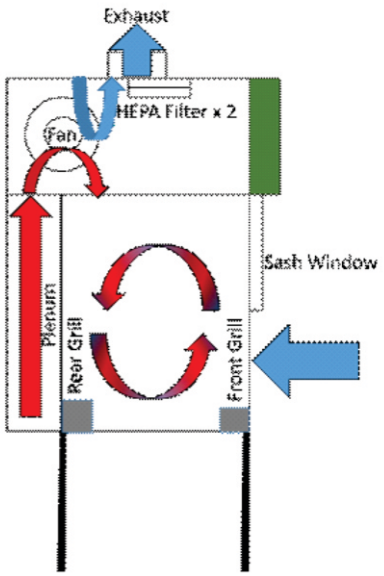


FIGURE 4-1. Class II Biological Safety Cabinet - Main elements

Secondary containment is achieved within the laboratory through inward airflow (negative pressure) and adequate filtration of exhaust air. All Class I and Class II BSC installation and testing must be in conformity with the National Sanitation Foundation NSF/ANSI 49-2004a: Class II (Laminar Flow) Biosafety Cabinetry standards (USA). The biological safety cabinets should be certified by the supplier at the time of installation. They also require certification after they are moved as well as on an annual basis. Accordingly, it is recommended that the institutional Environmental Health and Safety Office should be advised of any new installations to ensure they become part of the routine annual certification process.

Chemical Fume Hoods/ Canopy Hoods/

Canopy hoods i.e., overhead hoods are designed for personal work stations and intended to vent heat or local non-hazardous effluents (e.g. from autoclave venting). When the work involves manual manipulation or release of volatile materials, a chemical fume hood should be used.

LABORATORY SUPPORT AREAS/SPECIALIZED AREAS

Emergency Wash Devices

The emergency eye washes and showers must be clearly identified and easily accessible in the lab, preferably located within the immediate vicinity of potential exposures and supplied with warm water (Quebec regulation respecting occupational health and safety). Emergency showers and eye washes should ideally be located within 10 seconds walking distance (approximately 50 feet) of all work stations which require access to emergency wash devices. Modesty curtains are also recommended for emergency showers.

The standards recommended for design, installation and maintenance of the equipment by the American National Standards Institute Z-358.1, are summarized in the table.

Device	Design Features	Flow Rates	Temperature Control
Eye Wash	Single action, stay open activation 2 spray heads for simultaneous flushing of both eyes	1.5 litre per min for 15 min	Lukewarm water
Eye/Facewash	Single action, stay open activation 2 spray heads for simultaneous flushing of both eyes	11.4 litres per min for 15 min	Lukewarm water
Emergency Shower	Single action, stay open activation	75.7 litres per min for 15 min	Lukewarm water

SPECIALIZED AREAS

Cold rooms

Cold rooms are provided in large laboratories for storage of large quantities of samples, reagents and supplies. Cold room facilities that are intended for human access must fulfil the standard requirements for fresh air supply. Interior surfaces of cold rooms must be constructed of non-porous material to allow easy surface decontamination. Exit door latches must be fully functional from the inside.

Waste Collection and Storage Areas

Adequate space should be dedicated in each lab for waste storage, preferably near the front or exit of the lab. Large laboratory facilities may have dedicated hazardous waste rooms, which can be used for holding hazardous wastes awaiting collection by the hazardous waste management services. Requirements for such rooms can be variable according to the facility activities and workload. It is important that the hazardous waste management office is consulted on all construction or renovations related to hazardous waste areas.

Autoclaves

Autoclaves have complex vacuum and venting systems and thus special installation requirements. Furthermore, the growing awareness of the associated bio-hazards with the use of this important piece of laboratory equipment mandates that its location in the laboratory facility is selected after careful consideration of water supplies, waste drainage, ventilation and physical access for removal of autoclaved materials.

In case of cabinet type autoclave, the ideal space allocation would include: one meter on each side, 300mm on the rear and 2m or at least twice the length of any loading trolley at the front of the instrument.

- Drains: Autoclave drains should be able to resist steam temperatures up to 140°C. Domestic plastic waste pipes would melt at these temperatures if connected to an autoclave. Even with temperature resistant pipes, the joints could be undermined over time leading to accidents or leaks. This can be overcome by measures such as autoclave exhaust cooling; it is important to make appropriate arrangements at the time of installation following the manufacturer's instructions rather than after a costly leak.
- Water Source: It must be ascertained whether local access water can be used or whether treated (softened or reverse osmosis treated (RO)) water will be required.

SUSTAINABILITY IN LABORATORY DESIGN

A typical laboratory can use up to five times as much energy and water per square foot as a typical office building. High throughput clinical and research laboratories can be extremely energy-demanding for a multitude of reasons:

- Large numbers of air handling devices are in operation.
- A large amount of heat-generation by the equipment.
- 24-hour access may be a requirement for personnel.

- Requirement of fail-safe redundant power and energy backup systems such as uninterrupted power supply (UPS) or emergency generator power for irreplaceable laboratory operations/testing.
- The requirement to heat or cool one-pass air which is then exhausted.

However, careful evaluation of the energy, water and other requirements, from a holistic perspective, can help identify significant prospects for lab designs that incorporate sustainable options, in order to improve efficiency and maintain productivity while meeting or even exceeding health and safety standards.

Some key aspects of sustainable design are:

- Improvements to the interior and exterior environments, leading to increased productivity.
- Increased energy conservation and efficiency using alternate energy sources, sensors/timers for lights/ventilation operations etc.
- Reduction or elimination of harmful substances and waste generation.
- Recycling and increased use of products with recycled content.
- Efficient use of materials and resources and encouraging laboratory personnel to utilize available facilities responsibility.

RELEVANT CODES AND STANDARDS

Different agencies and organizations develop codes and standards regarding the design of research laboratories that serve as minimum requirements. Architects, engineers, and consultants should consider exceeding the applicable requirements whenever possible. These codes and standards can be accessed online.

Codes and Standards

- American National Standards Institute (ANSI) / American Industrial Hygiene Association (AIHA) / American Society of Safety Engineers (ASSE) Z9.5 Laboratory Ventilation.
- American National Standards Institute (ANSI) / International Safety Equipment Association (ISEA) Z358.1 Emergency Eyewash and Shower Equipment.
- Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) Standards.
- Guidelines for the Laboratory Use of Chemical Carcinogens, Pub. No. 81-2385. National Institutes of Health.
- National Fire Protection Association (NFPA).
- NFPA 30 Flammable and Combustible Liquids Code.
- NFPA 45 Standard on Fire Protection for Laboratories using Chemical.
- Quebec Regulation respecting occupational health and safety (Section 76; O.C. 885-2001). Available at: http://legisquebec.gouv.qc.ca/en/showdoc/cr/S-2.1,%20r.%2013.
- Unified Facilities Guide Specifications (UFGS)—Tri-Services, organized by Master Format™ divisions, are for use in specifying construction for the military services. Several UFGS exist for safety-related topics.
- United States Code of Federal Regulations, 29 C.F.R. § 1910.1450 "Occupational Exposure to Hazardous Chemicals in Laboratories" (OSHA).

BIBLIOGRAPHY

Biosafety in Microbiological and Biomedical Laboratories. 2009. 5th Ed. Department of Health and Human Services, Centers for Disease Control & Prevention and National Institutes of Health, US.

Laboratory Biosafety Manual. 2004. 3rd Ed. WHO Geneva.

NIH Design Policy and Guidelines, National Institutes of Health, US.

Chapter 5

Budgeting and Sustainability Issues

Ghulam Sarwar Pirkani, Bolan Medical College; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

In Pakistan, two systems of hospitals are functioning: public and private. Private hospitals are autonomous in planning, budgeting and marketing. The other type, public hospitals, are present at different level from tertiary care to secondary and primary level like district or tehsil hospitals and then the basic heath units. All public hospitals provide laboratory services, but quality assurance systems do not always exist.

The pathology laboratory is also an essential section of all the reputable hospitals. In Pakistan, private sector has provided enough funding to the laboratories, which has increased the creditability of these hospitals. Due to sufficient funding of these laboratories, the monetary income of hospitals has increased many folds, as the pathology laboratories are a significant revenue generating part of the healthcare system.

Financial support is the main pivot for continuing functions of any laboratory. The budgeting has to be very precise based upon the expenses incurred in the previous year(s) and forecasting future patient load. While preparing the budgets stocks available should also be considered. There is a trend to acquire latest equipment which may not be otherwise required. Such practices should be curtailed especially if no trained manpower is not available. Any specialized testing ability must not be acquired till the time there is actual demand. Pooling of lab facilities is a better choice. Moreover, the labs must be standardized according to the level of patient care. These are important concerns for sustainability.

STANDARDIZATION AND HARMONIZATION

The Maputo Declaration on strengthening of laboratory systems of 2008, called on governments, donors, and partners to ensure the product selection is harmonized across all programs. Standardization can lead to more efficient and rational use of laboratory tests and may streamline product selection, forecasting, quantification and procurement practices. Standardization is intended to achieve a set menu of tests (i.e., equipment and techniques) to be used at each facility at each level of the health system.

For assurance of equal standards within a laboratory setting, there is a need for a programme which may improve the operating conditions of these laboratories. The following steps are recommended to optimize purchasing and budgeting of laboratory equipment and reagents:

Purchasing Equipment for the Laboratory

In government laboratories, a provincial body purchases the equipment, and lab reagents. All purchasing contracts should include the following: 1) detailed equipment

specifications; 2) equipment installation agreement or detailed installation instructions; 3) manufacturer's instrument certification; 4) warranty terms and conditions; and 5) reagent cost estimates.

There are different types of laboratory equipment:

a) General Equipment: Instruments that are used in all types of laboratories such as water baths, heating blocks, centrifuges, pipettes, vortexers, mixers, washers and reader, incubators and refrigerators.
b) Specialized or dedicated: These are equipment required for a specific procedure such as PCR, ELISA and hormone assays etc.
c) Closed System: Some instruments only utilize manufacturer specific reagents. Generally, in the closed system quality of results is more accurate and reliable but such equipment is costly and specific to small number of tests.
d) Open System: In open systems, the end-user can select any manufacturer reagent. This type of equipment is usually less expensive than a closed system. The end-user also has flexibility to select good quality reagents and achieve better results. Unlicensed reagents, while occasionally less expensive, are of differing quality and may deleteriously affect the performance of the equipment.

Infrastructure for Laboratories

The following facility infrastructural and utility considerations are necessary before purchasing any equipment:

1. **Space:** Space must be adequate for performing requisite lab tests within the laboratory. Doors of laboratory should be free of obstructions and sufficient in size to permit entry of large laboratory equipment. Incubators, refrigerators and ultra-low freezers need extra space. Space requirements should be assessed prior to the procurement of any equipment.
2. **Power:** A continuous supply of electricity is necessary for operation of diagnostic laboratories. Most instruments and equipment function can get seriously compromised (blood banks, PCR analyzers) by a breakdown in electrical supply. Therefore, an uninterrupted power supply (UPS) is needed for all laboratories. If a high-tech equipment is required, then backup power source must be ensured.
3. **Water:** Clean water supply is also an essential need of all laboratories. Proper reagent preparation, washing, rinsing of glassware depend on a consistent supply of clean water. Distillation plant must be present in all laboratories.
4. **Environment:** The laboratory environment must be hygienic and dust free. Some equipment like chemistry analyzers and PCR analyzers require controlled temperature and a clean dust-free room for optimal operation. Adequate ventilation is also required to ensure the safety of laboratory staff.
5. **Waste Management:** Waste management is essential part of every hospital but the laboratory is the most common place for generation of maximum infectious material. There should be adequate policy and management for lab waste.
6. **Trained Human Resource**: For any equipment inducted trained HR is mandatory. If not, then the vendors need to ensure for proper training of the exiting manpower.

LABORATORY CONSUMABLES MANAGEMENT

For organization of laboratory certain points are necessary to be kept in mind:

1. All culture media, reagents, antibiotic discs and other consumables should be organized and stored according to manufacturer's recommendations. All shelves and containers should be labeled for ready access.
2. Fresh reagents should be stored in the back of shelves (“rotating stock”); older stock materials should be placed in front so as to avoid unnecessary expiration / wastage of consumables.
3. Items requiring quality control testing must be labeled as “awaiting QC”. After QC test passed reagents should be labeled as “ready to use” or passed QC.
4. Record the receiving date and also the date of opening of reagent bottle. The expiry date should be noted on reagent bottle with permanent marker.
5. Record the inventory of all reagent, media and consumables. Prepare inventory card for each item to record its number, vendor, vendor information quantity, count, lot number and expiry date.
6. Manufacturer's instructions or information leaflets, specifications of equipment shall be kept in a laboratory binder marked “equipment manuals”.
7. Package inserts of reagents and kits shall be kept in a laboratory binder marked “reagent / materials package inserts”. This binder must be accessible to laboratory staff at all times.
8. Standard Operating Procedures (SOPs): shall be kept in a laboratory binder marked “SOPs”. This binder must be accessible to laboratory staff at all times.

NATIONAL PROCUREMENT COMMITTEE

To avoid issues with procurement, it may be beneficial for notifying a national committee that prepares a national policy and guidelines for lab procurements. These may include: what items should be purchased and when it is needed; delivery and installation of equipment or supply of reagents. The vendors to be monitored for supply according to their previous performance; those having dubious supply record in past should be not allowed to participate in bid. The supplier should be responsible for delivery of items at site of utilization. In case of equipment, supplier must install the equipment and train the lab staff on its proper function. After installation would get the installation certificate from the in-charge of laboratory.

Provincial Procurement Committee:

In Pakistan, healthcare is a provincial subject therefore it is necessary that a provincial body must be formed for product selection, under guidance of national policy in all provinces.

Sequence of steps for procurement:

1. **Planning:** The following steps to be taken for procurement of diagnostic reagents and laboratory equipment.

- Need Assessment: The need for each type or level of laboratory is different

therefore procurement planning must be based upon need assessment.

- Technical groups at national, provincial and institute level must make plan according to the need assessment.
- Selection: Equipment specification and detail information about the products to be discussed and decision must be taken according to national and provincial policies. Public Procurement Regularity Authority (Pakistan) PPRA regulations have to be adopted for any procurement.
- Quantification: According to need assessment of the laboratory, the required quantity of reagents and type of equipment must be finalized. The annual quantity of reagents needs to be assessed, because in the public sector procurement is generally annual. Certain chemical reagents may be needed on a monthly or weekly basis, like blood analyzer reagents and washing reagents. Their required quantity should be assessed accordingly, while disposable reagents can be assessed on an annual basis.
- Budgeting: All procurement must be according to need assessment and priority list made according to available budget. All training and annual maintenance fees should be included in cost estimates because without proper training and instrument maintenance, expensive equipment may not be used optimally and even becomes non-functional within short period.

2. **Implementation:** In the public sector, procurement is managed by Medical Store Department (MSD) according to government rules. It is generally a committee comprising government officials who finalize the list of equipment and reagents. This approved equipment and reagent list is then published for a bidding process, whereby items with the lowest quoted price are selected. To ensure quality, it is necessary that detailed equipment specification with quality brand names be demanded. Both equipment and reagent costs should be considered when investigating the purchase of test systems, as some manufacturers will have low equipment costs but high reagent costs. The cost of reagents used in closed system equipment must always be assessed with cost of equipment. The authorized dealer should supply a company dealership certificate as many non-authorized dealers supply low quality supplies under false trademark of good quality manufacturers. Equipment training and maintenance agreements should be contracted with the authorized dealer. An annually renewable, 5-year agreement is recommended for most diagnostic instruments. PPRA rules and regulations must be followed for such supplies.

3. **Reagents Rental Basis:** This is a new practice by multinational equipment manufacturers. As the new auto-analyzers are introduced for analysis of large number of samples, the cost of equipment is generally very high, and hospitals cannot afford to buy such equipment, therefore the manufacturers place the equipment on reagent-rental basis and hospital has to purchase the reagents of manufacturer. Usually the equipment is of closed system type providing accurate result, but the burden of cost is shifted to the patients.

4. **Monitoring and Evaluation:** Quality control procedures should be in place to monitor performance of equipment and reagents. Quality control testing may be performed by the manufacturer; however, the laboratory holds the final responsibility of validating that equipment and reagents are performing at expected levels.

Diagnostic laboratory managers should be provided opportunities to obtain continuing education regarding budgeting and its principles.

BIBLIOGRAPHY

Maputo Declaration. Available at: www.who.int/diagnostics_laboratory/Maputo-Declaration_2008.

Public Procurement Regulatory Authority. Available at: http://www.ppra.org.pk/.

Section II:
LABORATORY SAFETY

Chapter 6

Laboratory Safety Essentials: Occupational Health and Safety, Vaccines, Personal Protection and Avoiding Laboratory Acquired Infections (LAIs)

Nasrullah Malik, Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore; Yasir Rafiq, Combined Military Hospital, Skardu

Safety in the laboratory is extremely important and necessitates that all workers be aware of potential hazards and how to deal with them. There are many different types of hazards within a laboratory; therefore, all workers must familiarize themselves with common types of accidents and how to deal with them, then it becomes easy to tackle any difficult or new situation or accident. Whenever any accident occurs in the laboratory, the supervisor or person in-charge should be informed, and the incident should be recorded in a log-book.



FIGURE 6-. Safety in the Lab (https://www.ck12.org/chemistry/laboratory-safety/lesson/Safety-in-Science-MS-PS/)

In serious cases, administration should also be informed. Different types of lab hazards are biological hazards, radiological hazards, chemical hazards, non-ionizing radiation hazards, physical hazards, and laser hazards.

It is helpful for laboratory personnel to familiarize with the first aid response in order to deal any accident occurring within the premises. At least one person among the lab staff must be thoroughly trained to provide first aid. Few examples of the expected emergencies and their responses are below:

TABLE 6-1 Emergency Responses

EMERGENCY	RESPONSE
Asphyxiation	Move casualty to fresh air; perform CPR only if medically necessary. Report any incident to appropriate supervisor.
Cut or punctured wound	Apply first aid by cleaning the wound with appropriate disinfectant, promote bleeding when necessary to help minimize risk of infection, and immediately report to proper supervisor.
Corrosive burn to eye	Thoroughly splash the eye with clean water and immediately report incident to appropriate supervisor.
Flooding and severe weather conditions	Safety of people is the top priority, only then consider the environment and equipment. Resume normal operation after thoroughly inspecting access routes, equipment and storage areas.
Electric burns	Wash with cold water for a few minutes and report to the supervisor.

GUIDES TO POTENTIAL HAZARDS

All laboratory personnel should be properly trained to identify hazards in the workplace. Many chemical, radiation, and biological substances may be marked with hazard identification symbols. This can alert laboratory personnel to use extra caution when handling these substances. Some of the common symbols include:



FIGURE 6- . Hazards in the lab (https://www.thinglink.com/scene/990903396468785153)

SPILL KITS

Spill kits are an essential component of any laboratory. Supervisors must ensure that they are kept up to date and readily available. All lab personnel must be familiar with the placement of the kit, ability to use it, and basic knowledge about the adsorbents and

disinfectants. For biological spills, an appropriate disinfection solution must be used for 20-30 minutes. A 10% hypochlorite solution is commonly used. For details regarding different types of spill see chapter 7 on waste disposal. To minimize spillages, we should use spill trays, good laboratory practice techniques and other liquid retaining techniques. Contents of spill kit include:

1. Disposable gloves;
2. Safety glasses;
3. Hazard tape;
4. Absorbent pads;
5. Plastic bags; and
6. Disinfectant (for biological spill)

CHEMICAL SAFETY

Main reasons of the accidents are lack of awareness and training of the personnel, improper storage of chemicals or poor control of ignition sources. It may also result from misidentification, wrong labelling, packaging, storage, handling or transport. It can result in fires or even drastic explosions. Chemicals are to be labelled as corrosive, explosive or inflammable and stored accordingly.

LIMIT AND CONTROL OF HAZARDS

All personnel should be aware of potential hazards before performing and test. Mixing chemicals can be dangerous and personnel should be aware of potential energetic or flammable reactions. If necessary, changes may be made to the reaction temperature, pressure or quantity. Also check whether the equipment is adequate to deal with the experiment. Exclude any extra person from the vicinity of the test/procedure. In all laboratories gas lines should be colour coded and should be regularly checked for leaks.

BIO-INCIDENT

Bio-incidents are defined as all incidents or accidents that occur while handling pathogenic organisms (biological agents) or the products derived from them; including genetically modified organisms, cell cultures and parasites that have the potential to cause infection, toxicity or allergy. They can be caused by technical failures or human errors.

BIOSAFETY

Biosafety as defined by WHO is the containment principles, technologies and practices which are implemented to prevent unintentional exposures to pathogens and toxins, or their accidental release. Biosafety level, BSL-2 levels are required for most clinical laboratories. They must have an eye wash station and should have a biosafety cabinet class IIA2 (See Chapter 4 for information regarding biosafety cabinets).

BIOSECURITY

Biosecurity is defined as the institutional and personal security measures to prevent the theft or loss of pathogens or toxins for any malicious use. Safety measures to achieve biosafety and biosecurity fall under four important topics:

1. Administrative /Leadership: Laboratory leadership is important in defining laboratory safety standards and providing a reliable resource for personnel to ask for help. For more information on the importance of Administration and Leadership, see Chapter 1.
2. Engineering controls: Laboratories can be designed with controls to help prevent the loss of biological material and mitigate the risk of an accident. For instance, this may include requiring a key or passcode to enter a laboratory, putting shelving at a reasonable height to prevent materials falling or spilling, redundant air handlers in case one set stops functioning.
3. Standard operative procedures or SOPs: SOPs are important in detailing how procedure should be conducted. For more information, see Chapter 2.
4. Personal protective equipment (PPE): PPE is important for protecting the user and the sample. Appropriate PPE should be worn at all times.

BIOLOGICAL RISK MITIGATION

The term biorisk is defined as a combination of the probability of occurrence of a harm where the source of harm is a biological material (CEN document). Analysis of severity and how frequently a laboratory staff is likely to be affected by this harm is referred to as biorisk assessment. Once the risk assessment has been performed, safety control measures are applied and then regularly monitored. This process of identification of hazard and steps taken to minimize the likely hood and consequences of harmful effects is called risk assessment and risk mitigation. Biological Risk mitigation includes four phases which helps to understand the risks and then plans accordingly to help mitigate the risk. Risk mitigation involves identifying the risk, assessing the risk, risk management and risk communication.

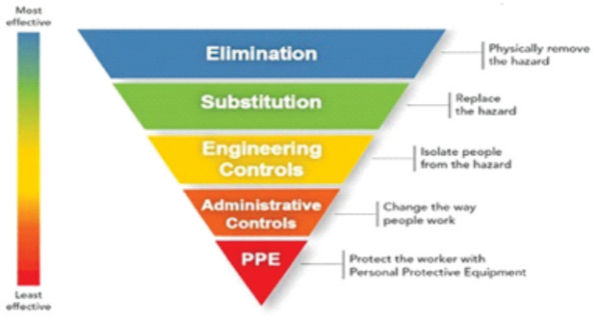


FIGURE 6- . Mitigation (https://www.ishn.com/ext/resources/Issues/2017/12-December/ISHN1217_F5_Welding.jpg?1512485603)

RISK IDENTIFICATION

It has been noticed that even commonly accepted or routine practices can result in serious infection. Marking of blood spots, mouth pipetting, transport of samples to the laboratory in corked or sheathed sharps, recapping of needles, eating, and smoking were all practiced commonly at one time, even in the reputed medical laboratories. All of these practices are now considered hazardous and are prohibited. Injuries with sharp objects continue to be identified as an area of concern. Sniffing plates to help identify organisms

and examination of bacterial culture plates with an eye-glass are considered unsafe. Laboratory staff should be aware of these risks and they should be guided to discontinue such practices that can inflict damage or infections.

The laboratory culture and practices are very important to prevent the occurrence and spread of laboratory acquired infections. Safe practices have to be ensured, SOPs have to be followed and any incident should be reported. There should be harmony and coordination between the staff working in the laboratory and the administration. Reporting the incident should be encouraged and incident surveillance should be given importance. The safe culture is ensured when a trust is developed between the workforce and the leadership. Following is the hierarchy of controlling lab hazards.

A **hazard** is any source or object that can cause harm; potential hazard in a clinical / research laboratory can be categorized as; a) biological b) chemical; c) radiological d) electrical e) facility related etc. Table 6-1 shows details under each category.

TABLE 6-2: Potential hazards in clinical/research labs

Biological Hazards: • Patient samples: Serum, sputum, pus, urine, stool etc. • Microorganisms: culture plates / vials, stored microorganisms etc. • Handling of animals • Animal body fluid • Genetically modified organisms / seeds	Chemical Hazards: • Solvents • Corrosives / oxidizing agents • Irritants • Carcinogens • Mutagens • Flammable
Radiation Hazards: • Ionizing agent • Ultraviolet agent • Infrared agent	Personal Hazards: • Expertise /skills • Manual procedures; streaking, pipetting • Mental stress • Physical stress • Multi-tasking • Untrained support staff (housekeeping)
Gases: • Gas cylinders / tanks • Gas lines under pressure • Flammable gas • Toxic gas	Electrical Hazards: • High voltage equipment • Live wires • Static charge
Facility Design Hazards: • Confined spaces • Overly cluttered benches • Poor ventilation • Noise / vibrations • Heat / cold stress	Equipment Hazards: • Aerosolisation: vortex, centrifuge • Sharps

TABLE 6-3. Laboratory activities with potential of aerosolisation or risk of inhalational exposure

Sample Processing: • Separating needles from syringes • Aspirating and transferring body fluids • Manipulating samples such as sputum, pus, other body fluids with syringes, needles, loops • Expelling air from syringes
Bench work: • Manipulating inoculation loops with live organisms • Sub-culturing / streaking live organisms • Spurting during loop flaming • Cooling loops in culture media • Harvesting and inoculating cell lines • Pipetting (expelling last drop from Eppendorf) • Vortexing and centrifugation
Performing Admin work: • Excessive traffic in workplace • Manipulating contaminated worksheets • Discarding used culture plates / tubes • Talking, coughing, sneezing / eating (including chewing gums) • Facility repair work

RISK ASSESSMENT

Before starting the experiment, try to know what sort of hazards you will be exposed to and what activities are involved related to those hazards. Safety data sheet is likely to help. Keep in mind any maintenance activity in the lab that may increase risk. Keep an eye on the people visiting the lab for security reasons.

RISK BASED CLASSIFICATION OF MICROORGANISMS

Microorganisms are classified into 4 groups according to their risks of causing disease and the treatment options available.

Group 1: Biological agents are unlikely to cause human disease in healthy persons.

Group 2: Biological agents can cause human disease and might be a hazard to workers but are unlikely to spread to the community, and there is usually effective prophylaxis or treatment available.

Group 3: Biological agents cause severe human disease and present a serious hazard to workers. They have the potential of spreading to the community, but there is usually effective prophylaxis or treatment available.

Group 4: Biological agents cause severe human disease and are a serious hazard to workers. They may present a high risk of spreading to the community, and there is usually no effective prophylaxis or treatment available. A partial list of microorganisms by category is shown in table below:

TABLE 6-4. Microorganisms by Category

Group	Bacteria	Viruses	Fungi	Parasites
1	No clinical organisms	No clinical organisms	No clinical organisms	No clinical organisms
2	*Bacillus* species (not *Bacillus anthracis*) *Corynebacterium diphtheriae* *Clostridium* species Enterobacteriaceae *Escherichia coli* *Mycobacteria* other than *Mycobacterium tuberculosis* *Staphylococcus* species *Streptococcus* species	Adenovirus Herpesvirus Influenza virus Calicivirus Coronavirus	All dermatophytes *Candida* species *Aspergillus* species	All human parasites
3	*Brucella* species *Bacillus anthracis* *Coxiella burnetii* *Mycobacterium tuberculosis* *Mycobacterium avium* *Francisella tularensis*	St. Louis encephalitis virus Hantaan virus Lymphocytic choriomeningitis virus Japanese encephalitis virus Western equine encephalitis virus West Nile virus SARS corona virus Prions	*Coccidioides immitis* *Histoplasma capsulatum* *Paracoccidioides brasiliensis* *Blastomyces dermatidis*	
4		Lassa virus Ebola virus Marburg virus Herpes simiae		

MITIGATION MEASURES – REDUCING THE IMPACT

Mitigation measures help to lessen the intensity of damage if an accident occurs. These include reducing number of persons in the lab and fire safety processes. An emergency plan should be ready and training should be given to workers to conform to it. Lab may be divided into different zones according to the level of the threat, especially if there is any hazard of fire or explosion. Electrical equipment should be positioned away from the expected splash area. There is a chance that spill will be followed by fire, hence other flammable liquids and dangerous chemicals should be stored at a distance. If there is a spill or fire, care should be taken that it does not spread to other explosive chemicals or dangerous materials. Risks posed by visitors and advantages of security guards are to be considered. Sanitary workers should know what to clean and what not to touch. They should know how to report any important incident or observation.

Safe Storage in Laboratory

All flammables should be stored adequately, identified and labelled properly and their Safety Data Sheet should be available. Heat, sunlight, moisture and other storage conditions should be adequate. Safety Data Sheet sent by the supplier or manufacturer needs to be consulted. It indicates the harmful effects of the material. For storage of microorganisms Pathogen Safety Data Sheet (PSDS) should be consulted. Most of Risk Group 3, Risk Group 4 and security sensitive biological agents require special access and inventory control for storage.

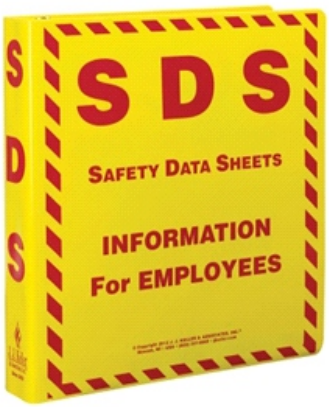


FIGURE 6- . SDS (https://www.jjkeller.com/shop/Product/Safety-Data-Sheet-Binder-15-Ring-Capacity)

Storage racks need to be sturdy and stable. If possible store hazardous material in a separate building or section with limited access and minimum quantities (less than 500 ml) and should be kept for minimum time. Cylinders should be stored in upright position and secured to prevent tilting.

People handling hazardous substances should be well educated and trained, containers should be robust, and the labels should be legible and long lasting. Smoking should be strictly prohibited in lab.

OCCUPATIONAL HEALTH SAFETY

Health problems can develop due to use of unsafe equipment, machinery, procedures, or activities. Use of hazardous materials, such as biological or chemical agents can be a cause of safety related problems. The principles of occupational health and safety include developing a policy, analyzing and controlling safety and health risks, training people, and investigating and recording health and safety incidents. Purpose is to reduce occupational diseases and injuries.

The workers have the right to know fully about the dangers involved in the work and they should obtain adequate training to deal with those hazards safely. They have the right to decline any unsafe work without fear of punishment.

Occupational medical services are to be arranged by the employer before the job starts. The medical health provider should have adequate knowledge of the relevant occupational risks and he/she should be able to get opinion of the experts. Potential

workers should know about the hazards they are prone to be exposed to and what they are supposed to do in case of exposure. There should be annual rehearsal for practice. Job related health injuries and illnesses should be recorded and then assessed annually. In case of dealing with dangerous pathogens, aim is also to prevent the spread of lab acquired infection to the community by diagnosing and treating early.

Annual medical evaluation of the lab workers is generally required besides any emergency or exposure. Workers should know the expected signs and symptoms from potential exposure to any infectious agent at the worksite. They should be encouraged to report to healthcare provider, if they have any illness related to potential biohazard. Objective is adequate treatment and recordkeeping.

There should be set protocol to respond to potential exposure to infectious agents e.g. by needle stick injury. There should be SOP for first aid, post-exposure prophylaxis and any diagnostic test required. First aid and wound cleansing are very important in management. Follow-up medical assessment should be encouraged. There should be a special protocol for injury and the healthcare provider should write following points in the medical incident report:

1. Expected infectious agent to which employee is exposed.
2. Route of exposure for example aerosol, needle or splash.
3. Place and time of incident or injury.
4. PPE, the employee was wearing.
5. Details of first aid provided.
6. Relevant personal medical history (diabetes, immunocompromised).
7. Vaccination status.

Post-exposure prophylaxis should be decided and managed well in time. It is sometimes not necessary to wait for the confirmatory lab tests. There should be a system to contact the subject-experts for consultation regarding vaccination or treatment if required. Before starting any post-exposure prophylaxis, it should be confirmed that exposure has occurred, and post-exposure prophylaxis treatment is not contra-indicated.

MEDICAL AND INCIDENT SURVEILLANCE

These two are very important components of lab safety, if any incident happens in the laboratory like a spill it has to be brought to the notice of the supervisor, manager or consultant and necessitates proper action, likewise in medical surveillance any medical condition or illness of lab staff should also be reported. It comes under administrative control.

There should be a “Workers Compensation Claim Form' that he should fill, if he feels he requires compensation because of injury. Supervisor should receive the incident report, confirm the circumstances and give advice. The incident report should be evaluated at appropriate levels to avoid exposure to such hazards in future.

It should be kept in mind that post-exposure serological testing usually requires two serum samples for comparison. First sample is collected immediately after exposure and second is collected about 4 to 8 weeks later. Four-fold rise in titre of antibodies is usually suggestive of infection. Serum may be stored at – 200°C or lower, if required to be tested later.

Health education is to be imparted to the employees as a part of occupational health. They are educated about first aid and specific risks and hazards. Training is required about handling sharps and contaminated linen. Education is to be given concerning donning and doffing of PPEs. Overall sanitation and hygiene, especially in the canteen or refreshing area needs regulation. In large organizations, medical records of the employees are maintained for keeping health standards and evaluation. Moreover, stress management and rehabilitation education are required especially for field workers.

Other factors to be considered are dust and noise pollution. Heat, radiation and vibrations are also irritants and need to be reduced. Consideration is to be given to family welfare and disaster management as well.

VACCINES

On resumption of employment, the organization should conduct a thorough medical examination of the new employee. Simply, a medical fitness certificate is an important requisite. This should include examining the new employee for any disease and recording any medication the employee takes. Moreover, any history of allergy and immunization should be noted. Immunodeficient and pregnant workers may need additional testing, like serology for toxoplasmosis and CMV. Other vaccines that may be considered are Hepatitis B, *Salmonella*, MMR, meningococcus, influenza, varicella and pertussis.

LABORATORY ACQUIRED INFECTIONS AND PREVENTION

Working in any kind of laboratory always involves various risks as the workers are dealing with different kinds of chemicals and microorganisms. So, it becomes really important to have adequate knowledge about the risks and the measures which should be taken to prevent them.

Laboratory-Acquired Infections

Laboratory acquired infections (LAI) are defined as all infections acquired through laboratory or laboratory-related activities regardless whether they are symptomatic or asymptomatic in nature. LAIs are among the occupational illnesses.

LAIs can arise in any laboratory especially those dealing with the infectious samples, clinical laboratories as well as in animal facilities, research and development facilities and food production installations. It is sometimes difficult to establish whether the infection has been acquired from the community or in the laboratory. LAIs are also of public health concern as an infected person from laboratory can act as a source of transmission and may present a risk of transmission to his family members, colleagues, citizens, or other relatives. This sets responsibility on the administration and the workers of the laboratory to comply with the safe practices to prevent LAIs among them as well as prevent any accidental release of live agents which can potentially threaten with severe negative effects on animals, humans and plants.

Laboratory safety involves many steps of the laboratory cycle, starting from the infectious samples' transport to the facility and continuing through the training of personnel, monitoring and establishment of safe working practices, proper use of equipment, material and reagents, safe storage of samples, and finally the terminal sterilization and destruction of microorganisms.

It is important, however to note that the laboratory testing cycle starts well before the sample reaches the laboratory (the pre-analytic phase of laboratory testing) and that exposures during the collection and transport of the specimen should also be considered. Infections experienced by phlebotomists as a result of needle stick injuries are also considered as LAIs.

How LAIs are acquired

LAIs result from occupational exposure to infectious agents. The most common route of exposure and accidental inoculation are the following:

- **Inhalation:** in the form of droplets less than 3 µm e.g., tuberculosis.
- **Percutaneous inoculation:** needle and syringe, cuts or abrasions from contaminated items and animal bites.
- **Contact:** between mucous membranes and contaminated material (hands or surfaces).
- **Ingestion:** e.g., aspiration through a pipette, smoking or eating.

Different studies have shown that the most common laboratory acquired infections in the recent past have been due to:

- *Brucella* spp.
- *Coxiella burnetii.*
- Hepatitis B, C and D viruses.
- *Salmonella Typhi.*
- *Francisella tularensis.*

The characterization of a lab worker's infection as laboratory acquired is usually retrospective and is based on the assumption that the likely exposure occurred while the person was working in a laboratory. A minor laboratory accident or event may be considered the possible exposure if there are no other pointing circumstances outside the laboratory that could be the cause of the infection.

SAFETY EQUIPMENT AND PERSONAL PROTECTIVE EQUIPMENT

Personal protective equipment (PPE) is the clothing or gear used to protect the user from specific hazards or hazardous materials. PPE does not reduce or eliminate the hazard but only protects the user. It is the last protection system to be used when administrative and engineering controls do not reduce risk to an acceptable level. Employers are required to train each employee who must use PPE.



FIGURE 6-5. PPE training being conducted

Employees must be trained to know the following:

- When PPE is necessary?
- What PPE is necessary?
- How to properly put on, take off, adjust and wear the PPE?
- Proper care, maintenance, useful life and disposal of PPE
- The limitations of the PPE.



FIGURE 6- . Protective Equipment (http://www.alocanta.com/clothes/in-eyalgroup-co-il-you-will-find-the-answer-for-the-question-how-will-protective-equipment-be-in-the-future)

The employer should document the training for each category of employees required to wear or use PPE by preparing a certified document containing the name of each employee trained, the date of training and a clear identification of the subject or purpose of the certification.

EYE AND FACE PROTECTION

Eye and face protection are extremely important when working in a lab and must be used if hazards are expected that could cause face or eye injury. Safety glasses and goggles provide protection against any accidental impact and splashes.

Even if the quantity of chemical is small, or engineering controls such as fume-hoods are used, eye protection must be worn. Other types of goggles offer protection from UV light and laser hazards. Face shields safeguards the entire face from projectiles and offers some safety from splashes. Goggles or safety glasses must be worn under face shields. It protects from microorganisms entering in eyes or mucous membranes as a result of accidental splash. It should have following features:

- Should allow unrestricted functioning of any other required PPE.
- Should be reasonably comfortable to wear and fit properly.
- Should provide unrestricted movement and vision.
- Ability to protect against specific workplace hazards.
- Should be cleanable and durable or disposable.

LAB COATS AND APRONS

Wear protective clothing that resists chemical, physical and biological hazards when contact may occur. Disposable outer dresses may be used when cleaning and decontamination of reusable clothing is difficult.

There are cultural norms as well like covering head with dupatta, scarf or niqab. It is recommended that disposable material sheets must be used *in lieu* while working in the labs dealing with highly infectious materials.

Lab coats

A lab coat or other protective clothing should be worn whenever chemicals or biological materials are handled. The lab coat will protect the user's private clothing and exposed skin (such as arms) from contaminants. Lab coats should be buttoned for best protection. Buttons should be preferably on one side. In our culture, some lab workers prefer to wear lab coat inside and outside the lab, as they feel more protected with lab coat. This is a big hazard as the lab coat gets contaminated in lab and can act as a source for the transmission of infections. So, if they have to put on the lab coat outside the lab they should have two different lab coats, one for the lab and the other one which they can use outside.

Aprons

They are required whenever splash or exposure on the chest or body of the worker is anticipated.

GLOVES

Wear gloves whenever handling hazardous materials, biological samples, chemicals of unknown toxicity, corrosive materials, rough or sharp-edged objects, and very hot or very cold materials. Use of gloves protect against skin absorption of chemicals,

thermal burns, chemical burns, and cryogenic liquid exposure. Choosing the appropriate type of hand protection may be a challenge in a laboratory. Gloves are made up of different materials and provide varied protection to the user. Lab staff and workers should be properly trained regarding the procedure of wearing and removing gloves. Latex gloves are usually utilized; in case of latex allergy, teflon gloves or other varieties may be used.

FOOT PROTECTION

Always wear closed-toe shoes in buildings where chemicals are stored or used. Do not wear perforated or open shoes, cloth sneakers or sandals in laboratories or where mechanical work is being performed. These shoes offer no barrier between the worker and chemical, biological and physical hazards. Leather shoes are likely to absorb chemicals and may have to be discarded if soiled with a hazardous material.

RESPIRATORY PROTECTION

Inhalation is one of the main routes by which injurious materials can enter the body. If an individual is exposed to any airborne concentration of such a harmful material, then it may affect the health. Masks are recommended as a protection against any aerosol generating procedure. Different types of masks include:

- Face Masks: a face mask protects the user from splashes but offers no respiratory protection.
- N95 Masks: offers the user protection from 95% of particles when worn appropriately. N95 masks must be **fit-tested** on each user to ensure that they function appropriately.
- N99 masks: offers the user protection from 99% of particles when worn appropriately. As with the N95 mask, this mask must be fit-tested.
- Powered air purifying respirator (PAPR): A PAPR supplies HEPA filtered air to the user.

These masks are designed as per the hazard and level of laboratory where an individual is working. Staff should be well aware of their use and limitations.

HAND WASHING

Hand washing is the simplest but extremely useful procedure to prevent the transmission of microorganisms and acquisition of infection in biomedical laboratories. Hands can be contaminated during handling of contaminated equipment, sample collection, handling of sample containers and touching of sample storage units. Simple hand washing with soap and water prevents the spread of infectious agents.



FIGURE 6-7. (https://www.who.int/gpsc/clean_hands_protection/en/)

Staff must be fully familiar with the appropriate technique required for hand washing. They should be trained how to wash their hands correctly missing no part of the hands. Although contamination can be reduced by the use of gloves, gloves alone are not completely effective. Hand hygiene can be performed with running water and either plain or antimicrobial soaps. Non-medicated detergent-based soap products and water alone do not disturb the normal skin flora but can have an effect on reduction of the transient hand flora, including both bacteria and viruses. The effectiveness is directly related to the duration of hand washing.

TRAINING FOR LABORATORY PERSONNEL

Any person who works in a laboratory must receive correct training to be aware of the possible hazards in the laboratory. It is the responsibility of the leadership and the administration to conduct training sessions for the workers so that they are conscious of the potential hazards and accordingly the preventive and safety measures should be adopted.

IMMUNIZATION

Immunization provides protection against some LAIs but should be considered inferior to mental alertness and good laboratory practices.

PROTECTION FROM SHARPS

Scalpels, broken glass, needles, and other sharps are generally associated with accidental injuries and in turn transmission of microorganisms if contaminated. Staff should be well trained on how to use the sharps and their disposal correctly. Appropriate usage of sharps containers diminishes the chances of injuries and transmission of potentially harmful agents. All sharps should be considered possibly infectious and should be discarded in puncture-resistant and leak-proof safety containers. The opening of proper discarder is one-sided so once the used material is introduced inside, it won't let out. Only one-third of the boxes are to be filled.

BIOSAFETY CABINETS

Biosafety cabinets are designed to offer safety to the worker while dealing with the infectious samples. They can protect the laboratory worker and the laboratory environment from splashes and aerosols and can also reduce the opportunities for sample contamination. Again, it is very important that staff should be properly trained to achieve maximum benefit out of these cabinets. BSCs and autoclaves come under engineering controls. For more information regarding the types of biosafety cabinets, see Chapter 4.

LAIs can range from simple self-limiting infection to very threatening condition. At times may lead to silent infections only to be discovered after damage has been caused. Safe lab practices, adherence to SOPs, use of PPE and proper training can however minimize all these risks.

OTHER ESSENTIALS

1. Staff should know the protocols in case of emergency including exit routes.
2. Staff should be familiar with the placing and use of fire extinguisher, first aid kit, eye-wash shower and the spill kit.
3. Staff should be acquainted with emergency telephone numbers and the location of the list of phone numbers.
4. Shoes should have good grip soles. Hair and clothing should not be loose or long.
5. Volatile substances should be dealt in chemical fume hood.
6. All unknown substance should be treated as hazardous.
7. Entry to the lab should be for authorized personnel only.
8. Food, beverages, tobacco or cosmetics must not be allowed inside the lab.
9. All accidents, injuries, fires, spills and near miss are to be reported.
10. Before leaving the lab, staff should turn-off all electric appliances, heaters, gas, and water. Moreover, identify and pack the waste adequately and store it at the designated place. Decontaminate work surfaces and equipment. Leave lab coats in the lab, close lab and lock the door.
11. There should be regular checking and maintenance of eye-wash station, fire extinguishers, fume hood, first aid kit, spill kit and chemical storage.

BIBLIOGRAPHY

Accidents and Emergencies. Health and Safety Essentials. Royal Society of Chemistry.

ASM Manual of Clinical Microbiology. 2015. 11th Ed.

Biosafety in Microbiological & Biomedical Laboratories. 2009. 5th Ed. Department of Health and Human Services, Centers for Disease Control & Prevention and National Institutes of Health, US.

Laboratory Biosafety Manual. 2004. 3rd Ed. WHO.

Online PowerPoint document: Essentials of Laboratory Safety. Available at: https://research.ucr.edu/ori/committees/ibc.

OSHA Guidelines on Personal Protective Equipment. 29 CFR Part 1915.

Chapter 7

Safety Systems and Safety Culture

Tim Trevan, Chrome Biorisk Management Consulting, U.S.

INTRODUCTION

Laboratory exposures that can potentially lead to laboratory acquired infections (LAIs) are far more common than actually reported. Not surprisingly, if people fear retribution for mistakes, they are reluctant to report them. So we have to create a work environment which focuses on the what went wrong and how to fix it rather than on the who did wrong and how to blame them. Furthermore, most people who make mistakes did not intend to but actually thought they were doing the right thing. In these cases, we have to ask the question, "What about the system facilitated them making the wrong decision or taking a wrong action?" This chapter focuses on the concept of safety systems and organizational learning that can bring safety culture in an organization.

SAFETY AND SYSTEMS

Systems

A system is a combination of operators, components, materials and information that performs a function or functions within an environment. There are many different types of systems, e.g. simple and complex; open and closed. They are found in every field of human endeavor; examples include production systems in factories, information and logical systems in mathematics and computing, engineering or physical systems, biological systems, cognitive systems, social systems, economic systems and cultural systems. For the purposes of this chapter, we shall focus on the systems typically found in laboratories, hospitals and vaccine production centres, namely management systems, production systems and socio-technical systems.

Management Systems = PDCA

Management systems are based around the concept of continual improvement. The basic steps are:

- Plan: Design and model operations, make predictions of what will happen for a given set of inputs;
- Do: Operate the system as designed, controlling to see that it is indeed operated as intended;
- Check: Measure the outputs of the system and check them against the predictions made in the planning stage;
- Adapt: Make changes to the design/model to improve the outputs/bring predictions more into line with the observed outputs.

Once the model and operating procedures have been refined, the management system requires formalization; recording and standardization; and developing standard

operating procedures (SOPs) to ensure consistent operations and outputs. A fully formed management system is a combination of:

- policies and procedures;
- clearly defined roles and responsibilities;
- certification of competence to operate the system (including training where necessary);
- systems controls to monitor and track performance and results; and
- regular review and improvement of the system and the model.

Within an organization, several different management systems exist side by side: production, quality control, financial control, performance, human resource, and safety to name a few. These can have competing objectives with each other, so it is important to ensure that each other system is in alignment with the safety system.

Safety System for Biological Laboratories

The European Union's Centre European de Normalisation has developed a standard for a risk management system for laboratories and other biological facilities, published as CWA15793. This is currently being transformed into an ISO standard (ISO35001). The central element of the proposed biological risk management system is modeled on the PDCA model described above and can be represented graphically as:

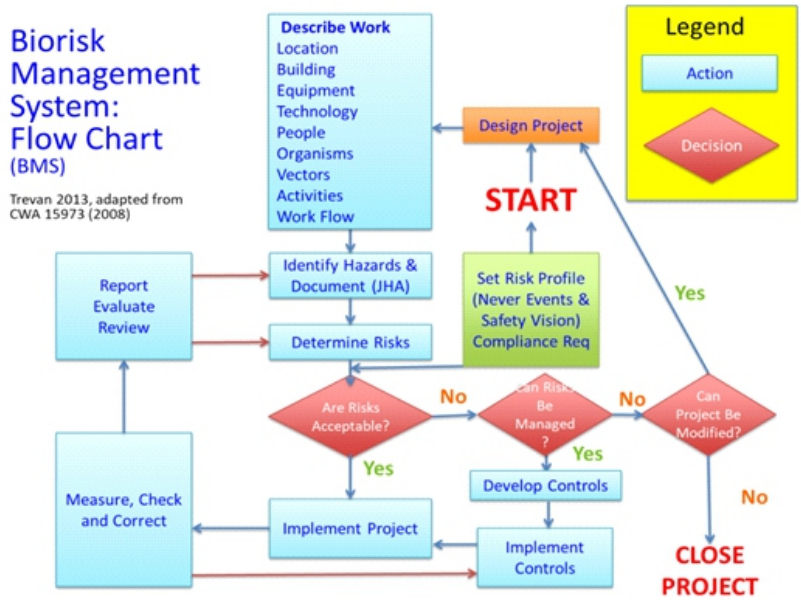


FIGURE 7-8. Flow Chart of a Biorisk Management System

Systems and Knowledge

Systems can be very simple or very complex. With regard to understanding systems and quantifying and modeling them for predictive purposes, it is important to distinguish between at least three families of systems: linear systems, chaotic systems and complex adaptive systems.

A linear system is deterministic, computable and measurable. By deterministic, we mean that if we know the system and the inputs, we can calculate the outputs. By computable we mean that it can be solved, that is an algorithm or equation exists for calculating an output if the input variables are known. By measurable, we mean that we can measure the inputs with sufficient accuracy and confidence to produce results of our calculations that are useful for prediction purposes. One example is clockwork, where the movement in one piece predictably and inevitably results in movements of every other piece in the system.

Chaotic systems are deterministic also, but they are sensitive to initial conditions. What this means is that tiny changes in the values of the inputs produce very large, non-linear changes in the outputs. We are unable to measure the inputs with sufficient precision, as changes in their values on scales smaller than what we can measure can drastically change the result. Thus, these systems, while computable, are not measurable and hence cannot be modeled to provide accurate quantitative predictions of what will happen with a given input (but they can be modeled to gain greater understanding of the system itself). The classic example of a chaotic system is the weather – if a butterfly bats its wings in Brazil will it unleash a cascade of events that result in a tornado in Texas, or will it simply cause a minor, temporary, local disturbance in the air which no-one notices?

A complex adaptive system has many feedback loops. Each loop is affected by the one prior; therefore, results at time t+1 are affected by how the system was at time t, results in time t+2 are affected by how the system was at time t+1 and so on. These systems are not deterministic and, like chaotic systems, are highly sensitive to initial conditions. They are defined by the interactions between the system's components, not simply by the components themselves. They are not computable, and they produce emergent properties that are simply not predictable from an understanding of just the components. An example of an emergent property is the sense of taste and smell – simply knowing the components, i.e. the chemicals, the nasal and tongue sensors and the brain's wiring, would not enable one to predict the emergence of a property not contained inherently in any of the components. The classic example of a complex adaptive system is evolution.

It is important to know the type of system you are analyzing or operating because it gets to the heart of whether you can use quantitative approaches or whether qualitative or semi-quantitative approaches are more appropriate. Complex adaptive systems get very complex rapidly as they grow in size. If each component is either present or absent, on or off, but can interact with every other component in any combination, then there are 2^n-1 possible combinations, where n is the number of components. So, a system with just 20 components that can all interact with each other has well over a million possible configurations.

However, if each component can be in multiple states (e.g. a computer with different operating systems; or a washing machine on different cycles; or a human in any of the many emotional states), then the number of possible system configurations rises at an even faster rate, at s^n-1 where n is the number of components, and s if the number of states each component can be in. Thus, with a group of humans each in, say, one of 8 possible basic emotional states, it only takes 7 people interacting with each other before the 'system' has more than 2 million configurations.

Another key aspect of understanding a system is being clear about the system's boundaries. Is it open or closed? And if trying to model an open system partially, how do you set the boundary of your analysis?

This is an issue in biosafety because, while what we do includes some purely technical systems – which can be linear and hence computable and measurable – the overall system is a socio-technical system because it involves people operating the equipment within a physical and regulatory environment and interacting with each other. Thus, while elements of the work of a laboratory, hospital or vaccine production centre might be linear systems, the work of the facility is clearly a complex adaptive socio-technical system.

The implication of this is that, while some clearly defined activities might be amenable to quantitative risk assessment, biological risk assessment for the facility as a whole is not, and efforts at best should be semi-quantitative (e.g. unlikely, possible, probable, very likely) or even qualitative (these are the things that we must do our utmost to avoid at all costs – the Never Events list).

THE LIMITS OF KNOWLEDGE

Andy Stirling at the University of Sussex has done some seminal work on how to think about whether systems are amenable to quantitative analysis and when they are not. In addition to evaluating the probability of an event and its likely impact, he suggests that we evaluate our confidence in our prediction of probability and our confidence in our prediction of what will happen and its impact. This, he argues, results in four different epistemological quadrants when dealing with risk assessment, corresponding to:

- quantifiable risk (confidence high in both probability and impact)
- uncertain situations (confidence in probability low and in impact high)
- ambiguity (confidence in probability high and in impact low)
- ignorance (confidence low in both probability and impact)

This can be represented graphically as follows:

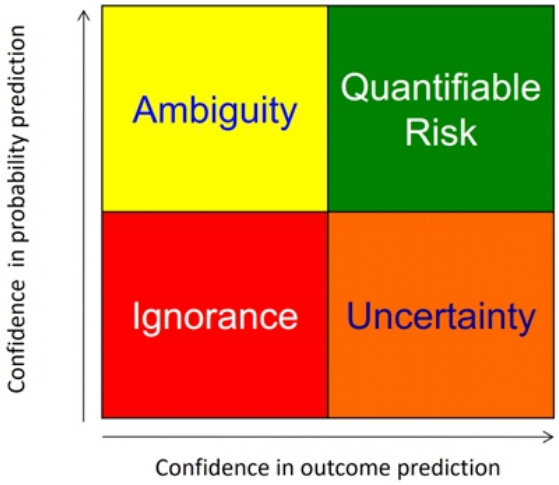


FIGURE 7-2. Risk and Imperfect Knowledge: The Four Domains of Knowledge (Adapted from Stirling, A. University of Sussex)

What are the implications of this for safety management systems?

1. Where knowledge of both probability and what will happen with what impact, quantitative risk management is appropriate and recommended;
2. Where it is known what will happen and that event's impact, but not the probability of the event, i.e. in conditions of uncertainty, sensitivity analysis and adaptation of plans based on the results of such analysis are recommended.
3. Where it is known that something will happen, but not what, or not the impact the event will have, then contingency planning and pre-accident investigations are recommended.
4. Where it is not known what will happen or its impact, and the probability of the adverse event is unknown, then adaptive risk management, e.g. operating to the principles of High Reliability Organizations, is the most that can be done.

Notable is that fully quantitative risk assessment is advisable in only one of the four quadrants; in the other three, it may not only be a waste of time and resources, it could potentially be very harmful, resulting in limited resources being spent on the wrong precautions and instilling a false sense of knowledge and safety.

SAFETY AND CULTURE

Laboratories, hospitals, veterinary practices and vaccine production plants all have multiple types of systems running at the same time. Some are simple, deterministic systems, others are complex adaptive systems, but the whole always operates within society as a complex, adaptive socio-technical system. Given the consequences of the release of pathogens into the community, these institutions all are in high consequence industries, and so it behooves them to adopt adaptive risk management approaches in addition to the more mechanical and quantitative approaches traditionally associated with biosafety.

High reliability organizations (HROs) operate in high consequence environments where failure can have catastrophic consequences, such as death, mass casualties, massive economic or infrastructure disruption, public panic or collapse of social order. They organize themselves deliberately in order to be able to operate consistently at extraordinarily high levels of safety while performing inherently complex and dangerous work in changing and treacherous environments.

Examples of HROs include civil aviation and off-shore oil exploration and extraction. HROs recognize that their systems are complex, adaptive socio-technical systems. They understand, therefore, that their systems are too complex to fully comprehend and will produce emergent properties – that is, totally unpredictable things will happen, and some of these will be dangerous. Given that the system cannot be fully comprehended, nor all of the undesirable outcomes envisaged, let alone quantified in terms of probability and impact, HROs cannot rely solely on quantitative risk analysis in order to operate safely. There will be many uncertain and ambiguous outcomes, requiring sensitivity analysis and contingency planning. But there will also be the unknowable unknowns, for which risk control requires adaptive management.

HRO practice adaptive risk management by applying five principles:

1. Focus on how the system can fail. Admitting that they cannot fully understand their system, they constantly try to imagine how the system could fail in order to avert the imagined failures and to improve resilience;
2. Sensitivity to operations, that is constantly observing the results of operations and knowing when small variances from expected outcomes could escalate to

serious failure, and when they are unlikely to do so, so that necessary interventions can be made before a situation deteriorates;
3. Recognition of expertise;
4. Complexity, greater emphasis on flexible response vs preventing all failures; and
5. Resilience.

At the core of the HRO approach, just as in the CWA 15793 Risk Management System, is continuous improvement. Experience in HROs show that, for continuous improvement to be sustainable and for an organization to be able to approach the excellence asymptote, seven different cultures are required. No one of these cultures is in itself sufficient to attain a culture of safety, as each play into the other. Operated together, these seven cultures make up a highly effective culture of safety.

1. **Informed Culture:** Leadership of the organization must understand the principles of HROs and of continuous improvement, and they must understand the management philosophies required to permit effective implementation of these principles.
2. **Just Culture:** Just culture means that people must be treated fairly and consistently. It does not imply that no-one should ever be punished or penalized. If someone deliberately endangers others, they should be punished. And if someone refuses to follow or is incapable of following safety procedures, they should not be permitted to do dangerous work. In the vast majority of cases – in excess of 85% of the time – workplace accidents are honest mistakes, made by people intending to do the right thing and thinking that they are. For such cases, a just culture focuses on learning from the mistake rather than seeking to blame a person. As a consequence, human error is never seen as a root cause, but as a symptom of an underlying systems failure.
3. **Reporting Culture:** In order to improve continuously, an organization needs data, and so it needs its people to report accidents, incidents, near misses and indeed any operation that does not go as expected. This is obviously closely related to a just culture: without a belief that they will be treated fairly, people will not report their mistakes or any other activity that was not performed perfectly.
4. **Learning Culture:** Everyone in the organization must understand that they should be learning continuously – that there is no reaching perfection, after which point no further improvements can be made. Even once an organization has reached the point of zero accidents, it can still improve its safety practices. A learning culture depends on there being an effective reporting culture.
5. **Culture of Flexibility:** Resilience is premised upon the idea that we cannot envisage beforehand all the ways in which a system can fail, and so we must build up our capacity to react with flexibility once an incident starts to unfold, with the aim of containing a situation before it gets unmanageable. Flexibility requires intimate knowledge of the system so that those responding to unfolding situations have the ability to make informed guesses as to how various response options will play out. Having multiple viewpoints and considerable experience operating the system are essential to flexibility. Both rely on an effective learning culture.
6. **Practicing Culture:** Knowledge is not of much value unless it is practiced. The behaviours of a just culture, a reporting culture, a learning culture and a culture of flexibility have to be enacted daily and become truly habitual so that, in the stress of an unfolding crisis, these behaviours are second nature and do not detract from response time.

7. **Culture of Accountability:** For any of the above to work, everyone within the organization must hold themselves, and their colleagues, accountable for acting safely and upholding the cultures. Everyone must speak up if they see unsafe behaviours or observe anything that might indicate an impending or developing incident. There must be no deference to authority, level of education or even years of experience. The expert is the person who observes a situation that needs to be responded to, and the person who knows how to respond - regardless of seniority or qualifications.

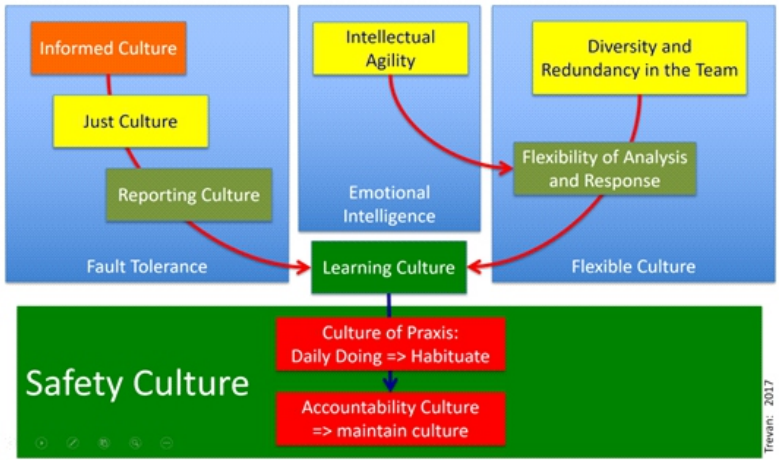


FIGURE 7-3. The Cultures that make up a Safety Culture

Culture does not magically appear because we want it to. It requires work, establishing shared visions and values, and developing attitudes of initiative, trust, curiosity and humility throughout to workforce – the ITCH for excellence. But once a strong culture of safety is established, the organization will reap the benefits of a workforce more engaged in and more proactive towards safety

BIBLIOGRAPHY

CEN Workshop Agreement (CWA) 15693: Laboratory Biorisk Management Standard. European Committee for Standardization 2011.

Chaos: Making a New Science. Gleick, J. 1987. Viking Press.

Complex Adaptive Systems: Computational Models of Social Life. Miller J.H. and Page S.E. 2007. Princeton University Press

Complexity: A Guided Tour. Mitchell, M. 2009. Oxford University Press

Deming, W.E. (1986). Out of the crisis. Cambridge, MA: Massachusetts Institute of Technology, Center for Advanced Engineering Study. p. 88.

Deterministic Non-Periodic Flow, E.N. Lorenz, *JAS.* 1963:20: pp130-14.

Just Culture. Balancing Safety and Accountability. Dekker, S. 2007. Ashgate Publishing

Managing the Risks of Organizational Accidents. Reason, J.1997. Routledge

Managing the Unexpected: Resilient Performance in an Age of Uncertainty. Weick, K.E., and Sutcliffe K.M. 2nd Ed. 2009. Wiley Periodicals Inc.

Stirling, A., Gee, D. Science, Precaution and Practice. Public Health Reports. 2003;117(6): pp. 521-533.

Thinking in Systems: A Primer. Meadows, D. 2008. Chelsea Green Publishing

Chapter 8

Biosecurity

Shamsul Arfin Qasmi, Karachi Institute of Medical Sciences
Julie Pavlin, National Academies of Sciences, Engineering, and Medicine, U.S.

INTRODUCTION

Biomedical laboratories work with diseases of humans and animals, analyze samples, and assist with epidemiologic, biomedical, and pharmaceutical research and development. They play crucial parts in the encounter against emerging and re-emerging transmissible infectious diseases such as Chikungunya, epidemic meningitis, *M. tuberculosis*, Avian influenza, SARS and many others. Every day, laboratories handle biological materials around the world for diagnostic workup and research; provide information about communicable infections; and advance novel skills and technologies to improve the state of education, science, and medicine. During this time of rapid advancement, many facilities are working with dangerous pathogens and their products on a small or large scale.

It is expected that laboratory personnel will act responsibly and take measures to protect the community and not expose themselves or the community to biorisks. Laboratory workers will follow safe working practices, and also keep samples secure from intentional release or theft for malicious use and will regulate an ethical code of conduct in relation to bioethics.

Although the work of these facilities holds many benefits for communities all over the globe, there are risks pertaining to working with infectious agents and their products which needs to be managed on a continuous basis.

HISTORY OF BIOTERRORISM

The use of biological agents as weapons dates back to the Middle Ages. Some more recent examples include:

- The Pancho Villa revolutionaries exploited Botulinum toxin (1910).
- The Mau separatists in Kenya used African milk brush toxin to poison steer (1952).
- An environmental extremist group known as Dark Harvest in the UK supplied *Bacillus anthracis* to pollute the ground of a political conference (1981).
- Aum Shinrikyo based in Japan tried to distribute Botulinum toxin at the US Naval Base at Yokohama and Yokosuka (1990).
- Although chemical in nature, Aum Shinrikyo also disseminated Sarin gas in the Tokyo subway killing 12 people and wounding hundreds (1995).
- The anthrax letter attacks in the US killed five persons and injured twenty-two (2001).

Laboratory Biosecurity & International Obligations

- Cartagena Biosafety Protocol 2003: The Cartagena Protocol on Biosafety to the Convention on Biological Diversity is an international agreement that aims to ensure the safety in transport, handling and use of laboratory modified organisms and genetically modified organisms that are byproducts of current and modern biotechnology which can have adverse effects on diversity.
- United Nations Security Council Resolution (UNSCR) 1540 calls for non-proliferation of weapons of mass destruction.
- Biological & Toxin Warfare Convention (BTWC): The BTWC comprises member states that have signed a treaty prohibiting the development of biological or toxin warfare agents.
- International Health Regulations (IHR): The IHR represents an agreement between WHO countries to work together for global security by building capacities to detect, assess and report public health problems.
- Pakistan
    - National Laboratory Biosafety & Biosecurity Policy 2017.
    - National Laboratory Policy 2017.
    - Pakistan Biosafety Rules 2005.
    - Pakistan Biosafety Guidelines 2005.
    - Draft BTWC Act 2018 is under process.

DEFINITION OF BIOSECURITY

Biosecurity is the principles and practice of containment that are applied to avoid the deliberate misuse or exposure to pathogens and toxins to humans and the environment. Pathogens and toxins have been used to intimidate and harm people, to disrupt society, and to hurt economies and the political situation. This has happened in spite of many international standards and guidelines which prohibit the use of biological weapons and any malicious use of pathogens. Even after the BWC banned the use of biological weapons, individuals have used pathogens as terror weapons. The anthrax attack in 2001 raised concerns in the international community to take laboratory biosecurity as a serious international issue.

In this regard, laboratory personnel and management must implement biosecurity in their facilities, but often biosecurity is not taken as seriously as biosafety. Biosecurity in the laboratory requires a dual responsibility for personnel; secure biological material so that it cannot harm others if inadvertently exposed, or a guarantee not to use the materials to deliberately harm others and also prevent others from doing so.

Laboratory biosecurity guidance, (WHO, 2006) approves a complete methodology for biosecurity required for laboratories. It states that it is the ethical, moral and technical duty of laboratory staff to protect the general community and to demonstrate that biological risks, which are intrinsic to laboratory work, are controlled with proper precautions for a safe global environment.

IDENTIFICATION OF VALUABLE BIOLOGICAL MATERIAL (VBM)

Laboratory biosecurity must provide more than preventing dangerous substances from being obtained by individuals, groups or organizations willing to propagate them for

harm. Apart from its primary role to secure Valuable Biological Material (VBM), it is also important that scientific, medical and pharmaceutical industries should also consider protecting materials with historical, medical, commercial, epidemiological or scientific value.

Scientists serve as custodians of valuable microbiological assets whose past and current value to science may be known, but whose usefulness in the future can only be guessed. Decisions to store materials should be taken with due consideration and consultation with the stakeholders. Examples of valuable biological material may include the following:

- Collections and reference strain types.
- Pathogenic microorganisms and toxins.
- Preparations of vaccines and other therapeutic products.
- Genetically Modified Organisms (GMO).
- Non-pathogenic microorganisms.
- Interplanetary (extraterrestrial) samples.
- Cellular constituents and chromosomal elements.
- Radio characterized (radio labelled) living compounds.

RISK ASSESSMENT

Risk assessment is the core of Biorisk Management (BRM) and therefore, implementing biosecurity should begin with assessment of risk. Determining and outlining risks at the facility will be helpful to establish parameters to meet the objectives of the biosecurity system.

DEFINITIONS

Biosecurity risk assessment is the likelihood of a pathogenic (Biological) agent being removed from a secure environment and the consequences from an outbreak after an intentional release of that agent. In other words

Biosecurity risk = (Potential for threat) x (Consequences)

Risk group	Facility needs	Examples
Very low risk for malicious use	No risk profile	Noninfectious forms of pathogens
Low risk for malicious use	Low risk profile	Small quantities of toxin, agents which can be transmitted by needle stick injury (NSI) or sexual exposure e.g., malaria, Hepatitis viruses, gonorrhea, E.coli, measles, mumps, P. aeruginosa and attenuated strains of other organisms used for vaccines
Moderate risk for malicious use	Moderate risk profile	Fungal agents (like *Coccidioides immitis*), *Salmonella* and *Shigella* sp, *Vibrio cholerae* spread through food and water
High risk for malicious use	High risk profile	*Bacillus anthracis*, *Yersinia pestis*, FMD
Extreme risk for malicious use	Extreme risk profile	Variola major virus, man-made pathogens with pandemic potential

FUNDAMENTALS OF BIOSECURITY

There are five units of biosecurity:

1. Strongly built Security: Physical procedures that minimize access to spaces within the facility which house equipment and biological agents. These include: perimeters and boundaries, access controls, alarms/observations.
2. Personnel Security: Measures established to minimize issues related to insider threats. These may include: screening of employees, classification of employees, employee ID cards, visitor escort policies.
3. Inventory Control: Measures established to identify when positive or negative discrepancies occur with biological inventories. These may include: inventory (what, why, how much), control (where), and accountability (who, when, for what).
4. Transport Security: Measures established to minimize insider and outsider threat during transportation. Security in transport is a mechanism to implement control to decrease the risk of theft from both inside and outside as well lessening theft while biological substances are transported between controlled zones. The transfer of biological materials can be facilitated inside a facility, between facilities, within a country and intercontinentally. These may include: internal transport policies and external transport policies.
5. Information Security: Measures established to minimize access to sensitive information and electronic controls. These may include: passwords, firewalls, policies minimizing use of USBs, policies regarding information systems (email, servers, internet use/downloads, software installation, etc.). (Fig. 8-1)

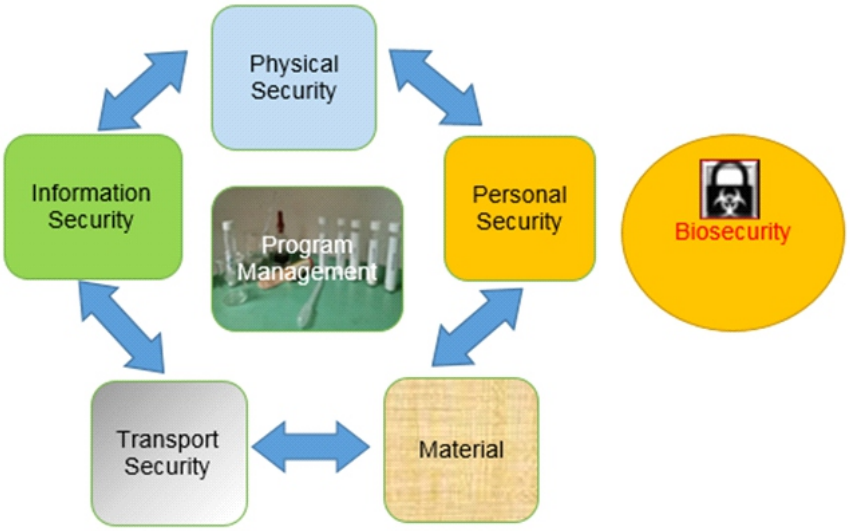


FIGURE 8-1. Fundamentals of Biosecurity

PROGRAM MANAGEMENT

Program Management is responsible to integrate, guide and oversee the laboratory biosecurity program and ensure it is implemented in a proper manner. It is the responsibility of the administration to safeguard every section of the laboratory biosecurity structure in a coordinated, steady manner. In this aspect, management is responsible for identifying the needs and prioritizing the requirements of the biosecurity system on the basis of risk calculation and assigning funds to achieve these objectives.

RECOMMENDATIONS

Biosecurity program management must be planned according to the biosecurity risk evaluation and assessment, which is the core to any biosecurity system. The biosecurity program is an overarching system that integrates biosecurity with biosafety and supports the overall biorisk management system. The roles and responsibilities for biosecurity management are divided among the following personnel according to the profile of the facility: management, biosecurity officer, lab manager, and staff. All personnel within a laboratory are responsible for biosecurity.



FIGURE 8-2. Graded approach for protection (Modified from: Laboratory Biosecurity Handbook. Salerno, R.M., Gaudioso, J.)

Most biological science laboratories are designed to check the insider and outsider threats. Physical security measures can help to enhance biosecurity. The use of graded zones within a laboratory is shown in Fig. 8-2. It includes:

- Property Protection Area: This is the outer most layer and can be used for low and very low risk agents. It is surrounded by the outermost perimeter of a facility, e.g., brick wall with iron gates.
- Limited Area: The limited area within an entire building can be selected as a restricted area. This limited area is appropriate for storing and dealing with moderate risk group agents. Access to these restricted and limited areas require permission and other restrictive devices such as an exclusive metal key, cipher such as a personal code, biometrics or a physical escort.
- Exclusion Area: It usually resides within the limited area; there can be many exclusion areas within the limited zone. The exclusion spaces are suitable for handling and stowing high risk group agents, including animals infected with these agents. It should have access control and intruder detection to make it more difficult to access. Only officials with authorization are permitted to arrive and depart the area without an attendant. Storage equipment like refrigerators and deep freezers may also be included in the exclusion area when positioned in a restricted zone and must have proper access control.
- Special Exclusion Area or Zone: The special exclusion area lies within the main exclusion area and is surrounded by barriers, gates, windows or other barricades that are the boundaries of this area. This space is recommended for placement of extremely hazardous agents. The special exclusion zone should be reinforced and strengthened to block the attempts of an adversary attempting to breach this area.

EMERGENCY RESPONSE FORCE

The emergency response force also plays a very important role in the security of biosciences facilities in case a breach or any other incident occurs. They should perform their duties according to a prearranged plan or agreement. In this regard, a clear understanding (in writing) between the laboratory and response force is mandatory to avoid confusion if the need arises for deployment. This agreement should define scenarios when force will be called and ensure the force is well trained in response protocols.

The response force may involve police, fire brigade services, 1122 emergency force in Punjab, or any other District, Provincial and National Disaster Management Authorities, or the federal security forces that can be called to manage an emergency state. Facilities or laboratories that contain and handle VBM and toxins should ensure that all related disaster management authority personnel are aware of the safety concerns and SOPs to be followed if an accident happens.

TESTING OF PERFORMANCE AND DOCUMENTATION

Performance testing conducted on an annual basis is recommended. After routine performance assessments are done, the outcomes should be reviewed and documented, and preventive and remedial corrective measures undertaken as necessary. These measures ensure a proper response in case of any incident. It can include repairing equipment, retraining personnel and amending existing policies and rules. It may also include audits.

TRAINING

Specific training and drills are critical for laboratory biosecurity. They are necessary to instill confidence in security measures in staff and employees and to make them familiar with these practices. There are different training modules for laboratory staff, laboratory supervisors, and especially response force for biosecurity.

Training includes information regarding limited admittance areas at the laboratory facility and the applicable procedures to access these zones. Information about policies and procedures for general physical security, employee security, data security and transportation security are provided to every employee deemed trustworthy. The trainings should be conducted on an annual basis, keeping in mind the objectives and needs of the facility.

NECESSITY FOR BIOSECURITY

With potential scenarios for the intentional release of pathogens, we must protect Valuable Biological Material. The existence of pathogens in the natural environment makes them accessible to anyone working in the field of biosciences, and it is a challenge to protect these items universally. However, given the viability and purity of many pathogens in the laboratory, the risk is greater if the terrorist obtains a pathogen from a bioscience facility than developing it through means other than the laboratory, and we must ensure proper biosecurity standards are in place to prevent this from happening. It is also difficult to prevent scientists or technicians from removing pathogens from the laboratory. However, scientists who work with these dangerous agents have a moral obligation to conduct themselves responsibly in order to to avert any mishap. It is also important to note that unnecessary security measures which can hinder the progress of research in a facility should be avoided so the research and development process is not impeded unnecessarily.

Besides providing a safe environment for laboratory personnel and the community, laboratory biosecurity has other benefits such as:

- Protecting valuable research and commercial items.
- Protecting populations and financiers.
- Complements laboratory biosafety agenda.
- Strengthens and fortifies the culture of biosafety.

BIBLIOGRAPHY

Applied Biosafety Journal. Available at: http://www.absa.org/resabj.html,.accessed.1/23/06;.6475.indb

Barletta, M. Biosecurity Measures for Preventing Bioterrorism, 2002.

Biosafety in Microbiological and Biomedical Laboratories. 2009. 5th Ed. Department of Health and Human Services, Centers for Disease Control & Prevention and National Institutes of Health, US.

Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma. 2003. National.

Kaplan, S. and Garrick, B.J. On the quantitative definition of risk. Risk Analysis 1981;1(1):11-27.

Keeping track of anthrax: the case for a biosecurity convention. Bulletin of the Atomic Scientists 58(3):57-62.
Laboratory Biosafety Guidebook. Qasmi, S. A., Ikram, A. and Kazmi, A. Publisher: Paramount Publishing Enterprise. 2013.
Laboratory Biosecurity Handbook. Salerno, R.M., Gaudioso, J. 2007.
Laboratory Biosecurity Handbook, Tucker, J. Biosecurity: Limiting Terrorist Access to Deadly Pathogens, United States Institute of Peace. 2003, Washington, D.C.
Laboratory Biosafety Manual. 2004. 3rd Ed. WHO Geneva.
WHO Laboratory Biosecurity Biorisk Management, 2006.

Chapter 9

Biorisk Management: Basic Concepts & Assessment Tools

Erum Khan and Sadia Shakoor, Aga Khan University, Karachi

This chapter is divided into three sections; the first section will introduce readers to the core concepts of biorisk assessment and mitigation in the context of clinical/research laboratories; the second section will outline the components of risk assessment; and the third section will deal with the tools and techniques for performing risk assessments and approaches to risk assessment – how to choose the correct method.

BIORISK ASSESSMENT AND MITIGATION

The term *biorisk* is defined as 'a combination of the probability of occurrence of harm where the source of harm is a biological material (CEN document). Analysis of the severity and frequency that laboratory staff are likely to be affected by this harm is referred to as *biorisk assessment*. Once the risk assessment has been performed safety control measures are applied and then regularly monitored. This entire process is called laboratory **biorisk management**.

COMPONENTS OF RISK ASSESSMENT

The components of risk assessment include:

Identifying Hazards:

Hazard is defined as a 'source, situation, or act with a potential for causing harm' (CWA 15793:2011). Potential hazard in a clinical/research laboratory can vary depending upon the type of the work done. In general, hazards in a typical laboratory are categorized under biological, chemical,; radiological, electrical, facility, personal, and equipment related (See Chapter 6 for more details).

Risk Characterization:

Once the hazards have been identified the next step is to ask simple questions related to each hazard items such as: What can go wrong? How bad and how often it can occur? and Is there a need for action to control such an occurrence from happening? For example, let's take a sputum sample as an identified biological hazard. The pertinent questions related to this hazard would be: What is the likely source of these samples? Where and how are these samples collected? What is the mode of transport of these samples from collection site to the diagnostic lab? Is there risk of leaking samples during transport? Where are these samples processed? What controls are available? What types of diseases are commonly transmittable (consider endemic diseases e.g. MDR-TB)? How is this hazard (sputum) discarded once the test is performed? Who discards it?

Risk Analysis:

Risk analysis is the likelihood of infection occurring. This exercise is carried out at all levels of diagnostic/research labs. As per good laboratory practices, the risk analysis can be conducted considering:

a. **Pre-analytical risk factors:** This component includes listing of all possible risk activities at the time of patient specimen collection at the laboratory or field site. Usually at this stage exact risk is not very clearly identified therefore standard precautions are generally advisable, such as the use of gloves and gowns. However some specific risk assessments can be made depending upon the situation. For example, if the laboratory is primarily linked to a specific program such as national TB control program dealing with sputum cultures only, then there is a greater risk of aerosol transmission of *Mycobacterium tuberculosis* (MTB) from suspected/diagnosed patients with open pulmonary TB to staff and other patients in the vicinity. The risk assessment in such cases should include the selection of appropriate personal protective equipment, such as the availability of appropriate facility controls such as a negative pressure control room for sputum collection. Alternatively, an open specimen collection site distant from routine human traffic would also be suitable. Similarly, blood sample collection poses highest risk of an injury with a possible needle stick injury or use of breakable glass tubes for sample collection. The availability of trained phlebotomy staff, the use of gloves, sharp discard bins, and unbreakable plastic blood sample collection tubes will minimize such risks significantly. Specimen transportation from collection site to the diagnostic bench site is another risk factor that needs thorough risk analysis. Use of appropriate labels/bar codes, unbreakable transport boxes, racks, etc. are important considerations. Individuals who are likely to be affected both directly and indirectly, including technical, administrative, and housekeeping staff should be identified. What is their level of involvement in the laboratory activity? Consider also the exposure of full/part time or night staff, cleaners, maintenance staff, contractors, patients, and visitors.

b. **Analytical risk factors:** Assess the competency, level of training of the technical staff, and laboratory design, including bench space. Untrained, incompetent staff and over-crowding of bench space, and improper ventilation may increase the risk of accidents and laboratory acquired infections. Special attention must be paid to activities with the potential of aerosolization and risk of inhalational exposure. Each step of specimen handling, processing, inoculation, and identification methods should be followed. The risk for bacterial culture based methods would be different from molecular based methods. Consider the activities, processes or substances in the laboratory that could cause harm. Review the manufacturer's instructions for potential hazards. Look back at accidents, illness and surveillance reports if available. Review the Safety Data Sheets for chemical hazards and suggested guidelines for safe handling (PPE, fume hood, etc.). Review the organism's/agent's properties. The result of risk assessments determines the requisite biological containment level in addition to other potential measures for protecting the personnel, community, and environment.

c. **Post-analytical factors:** Detailed review of process that involves specimen/hazard storage, and discard methods are elements of post-analytical factors. Detailed analyses of specimen/hazard storage, and levels of biosecurity measures will depend upon the risk category of organisms. Material

accountability/inventory is essential to track use, transfer, and destruction of biological agents. The objective is to know what agents exist at each facility, where they are located, and who is responsible for them. What are the safety and security measures in place and are they in line with the biosafety risk level of the microorganisms?

Finally, the methods of decontamination of all waste before removal from the laboratory and terminal discard by effective and validated method are essential considerations for assessing the risk of laboratory waste to the community and environment.

Risk Consequences:

Risks are 'evaluated according to the likelihood of occurrence and severity of consequences' (Fig. 1). This assessment may reveal potential risk factors at different levels, such as factors related to technical staff competency, lab design, ventilation system or waste management, etc. List potential hazards in a table format in columns and the likelihood of the occurrence happening in rows. Review critically in light of availability of control measure or no control measure. Each activity or task may have more than one associated hazard. Be as detailed as possible (Table 1).

TABLE 9-1. Risk Assessment Matrix

LIKELIHOOD		**CONSEQUENCE**	
	1. Insignificant	2. Moderate	3. Catastrophic
3. Certain	Medium	High	High
2. Possible	Low	Medium	High
1. Rare	Low	Low	Medium

Low risk: acceptable with frequent review of activity to assess if risk has changed;

Medium risk: some mitigation strategy needs to be introduced;

High risk: the risk here is unacceptable and work must not continue till urgent measures are taken to reduce the risk (to a medium or low category).

(Source: Modified and adapted from: https://eight2late.wordpress.com/2009/07/01/cox%E2%80%99s-risk-matrix-theorem-and-its-implications-for-project-risk-management/)

Hierarchy of Controls and Risk Acceptance

Once a risk has been identified and a consequence has been categorized (see the risk assessment tools), it is important to review the risk acceptance, and assess the control measures already in place. Proper enforcement of the control measures can ensure reduction in the risk. In case of inadequate measures, it should be reviewed in light of hierarchy of sequential hazard control: elimination, substitution, engineering control, administrative control, and use of PPE.

If a risk is assessed as catastrophic, and adequate control measures are not available, then the first step is to eliminate the hazard. However if elimination is not possible, then substitute. For example, substituting MTB culture in a BSL-2 lab with molecular methods can reduce the risk significantly. Adding further the engineering control use of biological safety hoods, using appropriate PPE, and establishing administrative controls may bring the scale down from unacceptable (elimination) to acceptable.

Monitoring

Putting in control measures are only effective if they are monitored and reviewed regularly. Availability of most sophisticated control measures may not prove effective if the staff is not trained to use them or do not abide by related policies. For example, untrained technical staff working in a biosafety cabinet may result in the blocking and/or disturbance of essential airflow systems, which may compromise the effectiveness of the system. Similarly, improper/irregular wearing of essential PPE may render risks at higher levels than accounted for. Therefore, regular monitoring and review of effectiveness of control measures implemented is of utmost importance for successful biorisk management.

TOOLS & TECHNIQUES FOR PERFORMING RISK ASSESSMENTS

How to choose the correct method?

There are many methods that can be used for risk assessment. Here, we suggest a few methods that are flexible and can be applied to various laboratory settings. Although methods for risk assessment may be quantitative, semi-quantitative, or qualitative, the risk assessment approach should focus on identifying all hazards of a laboratory method/process rather than focusing on quantitative measures which deviate from the actual exercise of proactively identifying and avoiding or mitigating hazards and risks (Table 1).

TABLE 9-2: Laboratory Risk Assessment Procedure: Template

Identify Hazard (HZ)	Activity associated with HZ	Risk Assessment			Control Plan	
		Control	Likelihood	Consequence	New control to minimize risk	Date
Sputum Sample	Processing for culture sensitivity test for MTB in BSL-2 lab by Junior staff	Wearing of regular mask	**Certain**	**Catastrophic:** MDR-TB transmission to technical staff and to community	BSC and engineering control, negative pressure	June 2018

Control: Current Control Method

Risk assessment begins with a thorough account of your laboratory and its activities. A laboratory processing only blood for blood counts will have very different risks (and therefore consequences and mitigation measures) than a laboratory culturing *Brucella* spp. The risks that need to be accounted for in such an exercise include safety of the workers, the environment and its management to avoid accidents etc. as well as the turnaround time for laboratory reports, quality of laboratory results, and cost for each test/process. The simple exercise of listing risks should be followed by a prioritization of all the risks (Example 1).

Prioritization of risks is based on tolerability of the consequences of each risk. Example 2 explains how risks can be prioritized according to their consequences and what may be considered tolerable in a BSL 2 laboratory. A likelihood matrix (Fig. 1) can guide as to which activities or processes are high risk and therefore need to be on high priority as the consequences may be unacceptable in terms of safety, environment, turnaround time, or cost; especially if an incident is more likely to occur than others.

This matrix can be used for prioritizing risks so that processes or activities with 'high risk' categorization can be mitigated or managed urgently. These would be risks likely to occur more often and with serious consequences.

In example 1, the laboratory in question may apply many methods, but qualitative methods are easiest to apply and cost the least. Although methods have their own strengths and limitations, due to their flexibility, this chapter focuses on a flexible qualitative method that may be applied to laboratories.

Example 1: Samreen is a microbiologist working in a BSL 2 laboratory that performs urine cultures. Among her most common bacterial isolates in the laboratory are *E. coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. Her supervisor in the laboratory has just undertaken a surveillance project where Hepatitis C antibody testing on serum separated from whole blood will now also be performed. She has received a procedural standard from a reference laboratory which includes step-by-step performance of the assay.

She wants to perform a risk assessment of this new activity in her laboratory so everyone is aware of the new hazards and risks they will face.

Samreen decides to list all the biosafety hazards her laboratory and her co-workers face with the new activity. She realizes that risks could be faced by all stages of the test, i.e., at the pre-analytic, analytic, and the post-analytic stages.

She has come up with a list of possible hazards to workers while performing the new Hepatitis C test. She then uses a fishbone diagram to divide the hazards into pre-analytic, analytic, and post-analytic stages.

Can you identify any more hazards?

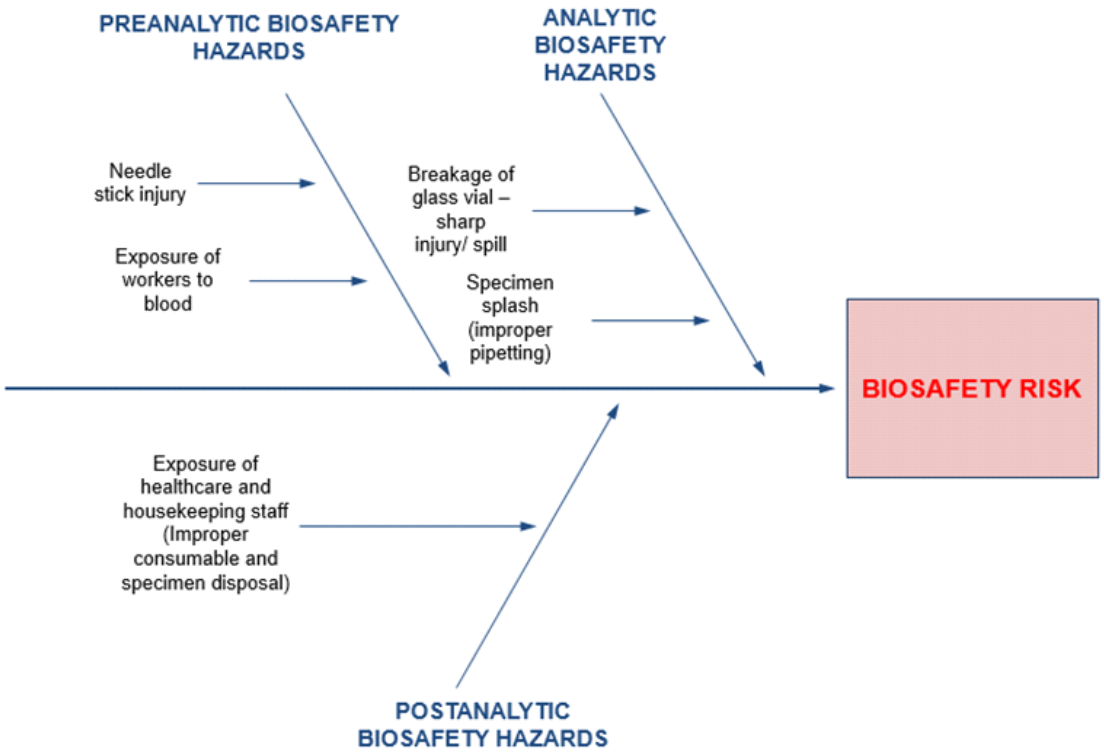


FIGURE 9-1. Biosafety Hazards

Example 2: Samreen then proceeds to make a risk matrix to analyze the likelihood and consequences from each hazard, and prioritizes risks based on this analysis. Your task is to help her out by performing the same for analytic and post-analytic hazards.

TABLE 9-3. Hazards in Pre-analytic Stage

Hazard	**Likelihood**	**Consequence**	**Risk**
Needle stick injury to worker	Possible (2)	Moderate (2)	MEDIUM
Exposure to spilled blood or dried blood	Possible (2)	Moderate (2)	MEDIUM

Help Samreen identify other hazards in the analytic and post-analytic stages and assess their risks (consider same conditions for testing as in your own laboratory).

TABLE 9-4. Hazards in Analytic and Post Analytic Stages

Hazard	Likelihood	Consequence	Risk
Pre-Analytic			
Exposure to blood due to glass vial breakage			
Post Analytic			
Exposure to blood due to inadequate disposal of biological material (blood)			

The Structured What-If Technique (Swift)

This method encourages workers to ask 'what-if' and allows identification of new hazards. This method may be employed once hazards have been identified and workers consider possible causes of hazards becoming imminent. This method may be applied to a number of laboratory activities including laboratory design, relocation, introduction of new tests and therefore expanding scope of testing, change in workforce, etc.

The Method: Example 3 demonstrates how a laboratory worker applies SWIFT to assess risks related to introduction of a new test on the laboratory menu. Each identifiable hazard suggests processes or activities where risks may be controlled or prevented. Workers first identify possible causes, list possible consequences, and then assess which preventive measures already exist and whether these are adequate to control the risk. If not adequate, further recommendations are considered to prevent or control these risks. A risk assessment through SWIFT may also be applied to older tests/ processes so identify biosafety/ biosecurity hazards and provides opportunities to avoid or control them.

Example 3: Samreen then carries out a SWIFT analysis for the risks with the highest scores first (High risk scores). She arranges a brainstorming session with her colleagues and they list possible things that could go wrong (What-Ifs) and then carry out an assessment of preventive measures that exist, control measures that can be triggered if the accident occurs, and what more can be done to more effectively prevent or control the risk.

TABLE 9-5. SWIFT Analysis

WHAT IF….	Possible causes	Consequences (result)	Existing preventive measures in lab	Recommendation for additional preventive measures
Glass vial with blood breaks!	Use of glass vial	Exposure of workers to blood and possibly hepatitis C virus	Worker training to be careful	Replace glass vials with plastic unbreakable tubes

Samreen then immediately contacts her manager with her assessment report. The manager files a request to the laboratory director to replace all glass tubes with plastic ones for testing immediately.

All risk assessment methods must also be followed by concrete steps taken to reduce or avoid risks (risk mitigation) and monitoring of the steps/actions taken to confirm the adequacy of these actions. This is also called the **AMP model** (**A**ssessment, **M**itigation, and **P**erformance) of 'BRM'.

Example 4 explains how Samreen applies the SWIFT method to a biosecurity risk in her laboratory and follows up with mitigation steps and monitoring to assess their performance.

Example 4: Samreen realizes that the patient specimens she receives for testing in her laboratory are all considered Valuable Biological Materials (VBM). She has learnt that all VBM need to be handled safely and secured in the laboratory so that there is no risk of leakage and potential spread of hazardous pathogens among the population; and that any leakage of specimens or pathogenic organisms is a biosecurity risk. Since her laboratory is a reference laboratory for Brucella, she realizes that the risk is highest of a Brucella clinical or reference strain being lost/ stolen/ disposed improperly.

Assessment: She quickly performs a risk assessment of a *Brucella* strain being lost or stolen, and recognizes that the occurrence is a possibility (likelihood) but the consequences will be catastrophic, therefore the overall risk is high. She therefore concludes that her first priority should be personnel education and training on biosecurity and waste disposal to minimize this risk.

TABLE 9-6. Risk Assessment, Brucella Strain Lost

WHAT IF….	Possible causes	Consequences (result)	Existing preventive measures in lab	Recommendation for additional preventive measures
Brucella reference strain is lost/ stolen	a) Irresponsible employee b) Stealing by unreliable personnel or unauthorized personnel with malicious intent	Possible Brucella infections among handlers Release to population with malicious intent	Laboratory access only to authorized personnel Background checks on all hired employees	Employee sensitization on biosecurity issues to avoid irresponsible loss and careful handling

Mitigation measures: She chalks out an employee certificate training course on biosecurity measures and effective infectious waste disposal techniques. She starts training her colleagues and other laboratory personnel and all laboratory employees complete this training in the space of three months.

Performance: The laboratory manager performs an **audit** of all employees to ensure that all those working in the *Brucella* laboratory are certified. The audit results suggest that the certificate course should be taken by new employees as well and that employee competence on biosecurity be measured.

BIBLIOGRAPHY

Awati, K. Cox's risk matrix theorem and its implications for project risk management. Available at: https://eight2late.wordpress.com/2009/07/01/cox%E2%80%99s-risk-matrix-theorem-and-its-implications-for-project-risk-management/.

Biosafety in Microbiological and Biomedical Laboratories. 2009. 5th Ed. Department of Health and Human Services, Centers for Disease Control & Prevention and National Institutes of Health, US.

Card, A.J., Ward, J.R., Clarkson, P.J. Beyond FMEA: The structured what-if technique (SWIFT). J Healthc Risk Manag. 2012;31(4):23-9.

Gribble, L.A., Tria, E.S., Wallis, L. The AMP Model. In: Laboratory biorisk management: biosafety and biosecurity. Salerno RM, Gaudioso J. (Eds) CRC Press; 2015: pp31-42.

Guidelines for Biosafety Laboratory Competency CDC and the Association of Public Health Laboratories. MMWR Supplement; Vol. 60 April 15, 2011.

Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories. Recommendations of a CDC-convened Biosafety Blue Ribbon Panel. Morbidity and Mortality Weekly Report Supplement; Vol. 61 January 6, 2012.

Potts, H.W., Anderson, J.E., Colligan, L., Leach, P., Davis. S., Berman, J. Assessing the validity of prospective hazard analysis methods: a comparison of two techniques. BMC Health Services Research. 2014;14(1):41.

Zaki, A.N. Biosafety and biosecurity measures: management of biosafety level 3 facilities. Int J Antimicrobl Agents. 2010; 36S:S70–S74.

Chapter 10

Emergency Response for Laboratories: An Outline for Preparation in Common Emergencies

Faisal Hanif, Bahria University Medical & Dental College; Umar Khurshid, Armed Forces Institute of Pathology; Maureen Sullivan, Minnesota Public Health Laboratory

EMERGENCY PLANS

"*The goals of disaster preparedness are to anticipate, mitigate and rehabilitate. All health professionals can and should contribute to this process. Among the most essential competencies are the ability to locate your institutional or office disaster plan, to understand your role in emergency; and to know how to communicate with patients, ancillary staff and governmental agencies during an emergency.*"

DiMaggio et al.

Emergencies can occur anywhere and importantly anytime regardless of the type of laboratory. There is no immunity to, even the smallest of emergencies and trivial of accidents, even for the most sophisticated of laboratories. Some accidents occur due to staff carelessness or inexperience; severe disruption of routine can also be the end result of electrical power failure, or natural calamities such as earthquakes or floods. Every laboratory person remains vulnerable to unexpectedly experience a situation mandating emergency response. The age-old dictum holds true that prevention is better than cure. The laboratory Emergency Response Plan (ERP) works around a meticulous plan, a thorough awareness of the working place surroundings, the known potential hazards and by thinking about what might go wrong. Mitigation of risks, a well-organized, maintained and clean work area has its benefits in the short and long term. Pertinent to this chapter it helps lab safety by ameliorating accidents and enhancing work efficiency.

Scripting and implementing emergency plans according to the resources and needs of the laboratory is a vital component of the good laboratory practices. Hence the performance, by each individual working in the laboratory, of "protocol mandated safety behaviour" is a must. These must be measured through audits at regular intervals both internally and externally.

Training and planning are required for successful dealing with incidents ranging from small scale localized emergencies to large scale emergencies. Emergency plans are always a part of the larger picture of laboratory practices which encompass the enforcement of good laboratory protocols. This includes staff training and evaluation, maintenance of the laboratory facility and equipment through preventive maintenance schedule and vendor provided services, and awareness of potential physical, procedural and chemical hazards and their mitigation.

Since the Global Health Security Agenda Action Packages require the public health labs to perform additional responsibilities in time of need and emergency, it is a must that the laboratory director and the staff of the lab associated with the additional responsibilities know about the emergency operations plans. Mechanisms for shifting to performing these additional duties shall be defined. This surge capacity plan has to be laid out so that it is synchronous with the Continuity of Operations Plan (COOP). Emergency Operations Plan (EOP) has to be instituted with formulation of SOPs laying out the mandate including the chain of reporting with timelines.

This ERP can broadly be divided into four sections:

a. Mitigation phase.
b. Preparedness phase.
c. Response phase.
d. Recovery.

Mitigation Phase

All emergency plans are based mainly around the type of facility and work being carried out in that laboratory. Preplanning for any emergency revolves around the specific tasks being performed.

The first step is to identify individual/specific tasks. A task is every single step carried out by the laboratory technician in the execution of the overall procedure. Identifying a task is vital as it forms the basis for emergency response. This may be as trivial as opening up of vacutainers or as complicated as culturing microorganisms. A thorough breakdown of the procedure is a must to identify potential hazards.

When the individual tasks are enumerated, potential hazards associated with the specific task are identified. Routes for exposure/entry to human body are explored; for this an extensive literature search is suggested. To begin, prioritize these risky laboratory activities based on the likelihood of accident/emergency. A history of emergencies/ accidents and events will be helpful in determining the incidence of such activities. Special focus should be placed on Biorisk mitigation of Valuable Biological Materials (VBM) (See Chapter 6 for biorisk mitigation).

Hazards both short term and long term are identified for each task and so are the current personnel, administrative and engineering controls associated with each task. Risk assessment is done primarily for the sake of focusing attention and energies. The risk assessment is done to determine the level of risk as, high, medium and low. A risk matrix is prepared taking into consideration the likelihood and consequence of a hazard. More the likelihood and severer the consequences, more extreme is the risk. Hence these are to be avoided at all costs.

To counter all the expected risks, a risk control plan is then outlined. The recommended controls (procedure related, personnel, administrative and environmental) are listed. Timeline is set to complete the control items identified. If procedures are already being done, risk assessment will dictate whether these can continue or be temporarily suspended until adequate safety measures are in place. In high risk procedures, work has to be halted and resumed only when the risk is mitigated or reduced sufficiently. The new control measures which are introduced may require changes to the already existent procedures or use of special equipment or facility. Maintaining the control

items, inventory making, stocking, turnover and addition remains the responsibility of the emergency handling team and the facility manager. In addition to the emergency response, team should be aware of the control items – every person working in the lab should be fully aware as to the placement, utility and safe use.

Preparedness Phase

The lab management is responsible to define, evolve and establish relevant SOPs for any emergency. The emergency responses may be at the individual level or may require team work within the laboratory or between laboratory personnel and other agencies. Individuals should be nominated in the SOP for specific tasks. If personnel do not understand their role during an emergency, this may add more confusion during crisis time. This can be addressed in exact plans being charted earlier in which a focal person is assigned specific duties along with the team members and the resources they would need to counter any of the emergency situations.

When the likely accidents/ emergencies have been outlined, management should develop a list of material and other resources needed to respond to the emergency and then procure those items. The inventory preparation is not a one-time activity as it will include items with definite shelf-life and proper storage condition requirements, therefore inventory management is mandatory. The focal person and the team responsible for handling the emergency on a 24/7 basis should be fully aware of the placement and use of these emergency items. Training for every person working in the lab, should be conducted yearly and updated regularly.

Training forms a core component in planning as the emergency equipment and supplies may not be in routine use and hence any unfamiliarity with the procedure and equipment may lead to loss of critical time. The focal person and the team have to be conversant with the procedures and protocols to be followed in emergency and should have sufficient knowledge, skills and depth as to accommodate loss of any member within the team. The team should meet on regular basis and document the proceedings. This may also mean bringing about a change in the storage or placement of different equipment, reagents and emergency response materials. The new control measures have to be meticulously developed and integrated into the existing protocols.

The communication plan should be clearly understood as it can have an effect on the short as well as long term effects of the emergency response. The procedures once developed have to be rehearsed successively with each team member cognizant of the responsibility assigned. The preparedness phase involves making a final action plan with the human and material resources. As it is a live document and individual may be moving in and out of the concerned laboratory, an updated list of the response individuals has to be maintained and on-call individuals be apprised as per SOPs. Mock exercise for various scenarios is essential as it may involve other departments like police, fire fighting etc. These would particularly be involved in natural calamities such as earthquakes or man-made disasters. Coordination is vital and has to be practiced beforehand. A plan must exist for a properly validated bi-annual or yearly full-scale mock exercise involving all the elements.

Response Phase

"Chance favours the prepared mind"- Louis Pasteur

This is the phase critically deciding the outcome of the event, the organization's reputation and its ability to recover smoothly. Whether or not an organization is highly reliable or otherwise depends on the initial management of the emergency. The eventual response will only gauge the extent to which one has prepared the individuals and placed systems in it which don't buckle over even under sustained and heavy calamity. Only a meticulously prepared, properly organized and well-rehearsed plan would succeed. Every member of the team has to be clear on the role and responsibility one has to undertake during the crisis hour. Coordination and coherence are vital to a favourable outcome as this phase may employ individuals from outside the lab and working environment. The response phase may be further complicated with the non-availability of other agencies, facilities, manpower and material aid on which previous exercises were modeled upon due to the very emergency which took place. Hence alertness and utilizing of human and material resources and putting these to use in the given circumstances is a test of the depth and management of the local focal person who is in charge in such a situation. All efforts have to be made in a safe and secure environment for the responders.

In addition, emergencies may take on different forms and the resources required may not be readily available. In a worst case scenario, alternate arrangements may be made; therefore, not only a knowledge of own resources is essentially required, but alternate sources of emergency workers and material is also prudent to put a system back on track immediately with minimum interruption. Learning is a vital part of any experience and whatever deficiencies or loopholes were encountered or observed have to be properly documented. This will not only help the very organization in which the accident /disaster happened but will also be a source of guidance for others who can look at the details of the event, learn from it and perhaps contribute to the improvement of the organization. The eventual response is all a mix of knowledge and its application, learning and in part the knowledge gained by others' experiences applied into the current situation. Training will play an important role in developing emergency response plans.

Recovery Phase

Continuity of laboratory operations is the ultimate aim of a good emergency plan. This can be achieved within the facility housing the lab or has to be setup temporarily in another location. Whichever place is best suited to meet the functionality aspect, specific priorities and critical functions have to be identified beforehand as well as vital equipment. A minimum amount of supplies and manning level for the lab has to be established. A good emergency response plan will always account for supplies and manpower beyond the capability of the own organization to keep the system running at a near normal/ bare minimum.

The emergency response plan remains a living document which has to be reviewed and updated in accordance with the emerging needs, national and international guidelines, change in the facilities of the lab and a need to need basis.

The intent of this chapter is not to give precise detail of every emergency and actions to be taken in that emergency; however, the following broad-brush stroke identifies the categorization of the major lab accidents and the ERP.

MAJOR LABORATORY ACCIDENTS

When planning for emergency response procedures, leadership/management should keep in mind to protect laboratory equipment and research material from damage or loss. This can be accomplished by taking appropriate precautionary measures that will help minimize the impact of damage from fire, severe weather or electric failures.

Leadership can prepare a lab emergency plan that will work for various emergency scenarios. This plan should be shared with concerned persons. Everyone must know the responsibility individually.

There are many other types of emergencies which may include environmental and natural disaster emergencies that may occur in the laboratory but here we focus only on accidents like

- Biological Spillage.
- Chemical Spillage
- Fire and Explosion.
- Personnel Injury/ Medical Emergency.

1. Biological Spillage

The first step in cleaning up a biohazard spill is to follow established procedures as described below to minimize the potential for exposure. Fill out and submit Incident Report Form (see Appendix 9) to Facility Manager for all incidents.

1A. Major Biohazard Spill (>10 ml)

1. Raise a spill alert immediately to apprise all staff working within the laboratory.
2. Stop all activities and prepare to leave the laboratory immediately for the anteroom/designated area.
3. Remove contaminated clothing, turning the exposed area of the clothing inward and discard it into a biohazard bag for autoclaving. If possible wash all exposed skin with antiseptic/soap and water.
4. The emergency evacuation route is not to be used unless the normal exit doors through the anteroom/designated area are not accessible.
5. Post a “No Entry” sign on the door of laboratory. Allow the aerosol to settle for 30 minutes.
6. Attend to injured or contaminated personnel in the anteroom.
7. Inform the Facility Manager. Exposed personnel will be directed by the Facility Manager for first aid or post-exposure prophylaxis.
8. Before cleaning up put on appropriate PPE (gloves, goggles, shoe covers, Tyvek suit/long-sleeved solid-front gown, N95 mask). Assemble clean-up equipment: fresh 1% virkon or 1% sodium hypochlorite, forceps, paper towels, biohazard bags, etc. – all must be available in the spill kit.
9. Pick up broken sharp items with forceps and discard into sharp box. Cover the spill with paper towels to avoid forming aerosols.
10. Operator must prepare fresh disinfectant solution and cautiously pour it over the spillage area. Pour disinfectant over the paper towels initially around the edges of the spill to avoid further aerosolisation, then into the spill. Avoid splashing. It

must be given at least 20 minutes' contact time. The contact time between infectious agents and disinfectant can vary but should be listed on the Pathogen Safety Data Sheet.

11. Spilled material contact-time with the disinfectant must be for a minimum of twenty minutes.
12. Wiping of the spill should be done with paper towels and it must always be from the periphery towards the center.
13. Once done fresh towels soaked with disinfectant must be used to re-clean the spill area.
14. All used towels and PPE worn must be placed in a plastic bag as infectious waste and then sent for autoclaving (90-minute cycle, 121°C for 20 min).
15. Hand washing to be carried out with antiseptic solution/soap.
16. Remember to document the incident mentioning detailed information for future reference.

1B. Lesser Volume Spill (<10 ml)

1. Raise a spill alert immediately to apprise all staff working within the laboratory.
2. Stop all activities and prepare to leave the laboratory immediately for the anteroom/designated area.
3. Post a “No Entry” sign on the door to the laboratory. Allow the aerosol to settle for 30 minutes.
4. Appropriate PPE including double gloves must be worn.
5. Cover the dirty spillage area with paper towels.
6. Operator must prepare fresh disinfectant solution and cautiously pour it over the spillage area. Pour disinfectant over the paper towels initially around the edges of the spill to avoid further aerosolisation, then into the spill. Avoid splashing. It must be given at least 20 minutes' contact time.
7. Spill must be wiped by working from the outer area towards the center by using appropriate size towels (paper).
8. All used towels and PPE worn must be placed in a plastic bag and sent for autoclaving (90-minute cycle, 121°C for 20 min).
9. Hand washing to be carried out with antiseptic/soap solution.
10. Remember to document the incident mentioning detailed information for future reference Appendix 9

1C. Biohazard Spill in Biological Safety Cabinets

A spill inside the biological safety cabinet does not pose risk to others in the lab or to environment if BSC is functional and on at the time of spill.

1. Raise a spill alert immediately to apprise all staff working within the laboratory.
2. Allow the BSC blower ON for at least 10 min. Appropriate PPE including gloves must be worn.
3. Operator must prepare fresh disinfectant solution and cautiously pour it over the spillage area. Pour disinfectant over the paper towels initially around the edges of the spill to avoid further aerosolisation, then into the spill. Avoid splashing. It must be given at least 20 minutes' contact time.
4. Spill must be wiped by working from the outer area towards the center by using appropriate size towels (paper). Wipe clean wall, top and underside of tray and exhaust grille.

5. Put all waste in the bag for autoclaving (90-minute cycle, 121°C for 20min).
6. Wipe clean the BSC with 70% alcohol and leave for 10 min.
7. Notify the Facility Manager of spill. It may be necessary to decontaminate the interior of the cabinet.
8. Remember to document about the incident mentioning detailed information for future reference Appendix 9

1D. Biohazard Spill in a Centrifuge

1. Raise a spill alert immediately to apprise all staff working within the laboratory.
2. Stop all activities and prepare to leave the laboratory immediately for the anteroom/designated area.
3. Turn the speed of centrifuge to zero. Allow the aerosol to settle for 30 minutes before opening the centrifuge. Post a “No Entry” sign on the door to the laboratory.
4. Inform Facility Manager before continuing with clean-up procedure.
5. Before cleaning up put on appropriate PPE (gloves, goggles, shoe covers, long-sleeved solid-front gown, N95 mask). Assemble clean-up equipment: fresh 1% virkon or 1% sodium hypochlorite, forceps, paper towels, biohazard bags, etc. – all available in the spill kit.
6. Open up the safety buckets inside the BSC. Place spill contents in a jar containing 1% virkon solution for at least 20 minutes.
7. Soak the contaminated buckets in 1% virkon for at least 20 minutes
8. Rinse the bucket with water thoroughly and autoclave before re-use.
9. All surfaces inside and outside of centrifuge must be disinfected immediately with 70% alcohol.
10. Remember to document the incident mentioning detailed information for future reference (Appendix 9).

2. Chemical Spillage

1. Raise a spill alert immediately to apprise all staff working within the laboratory.
2. Stop all activities and prepare to leave the laboratory immediately for the anteroom/designated area.
3. Inform the Facility Manager.
4. Wear appropriate PPE.
5. Select appropriate neutralizer / absorbent agent from the chemical spill kit.
6. Spill must be wiped by working from the outer area towards the center by using appropriate size towels (paper). Neutralize chemical spill and collect residue into bag.
7. If the solution spilled also contains a biological pathogen decontamination may be necessary. If the residue contains potential infectious agents, decontaminate the residue with an appropriate decontamination solution. Contact time is at least 20 minutes.
8. Radioactive waste must be left in transparent acrylic box (Perspex) if available in the laboratory to decay (to negligible proportion) before disposal as hazardous waste.
9. Wipe clean the area of spill with sponge or paper towel soaked in 1 % sodium hypochlorite.
10. Dispose decontaminated waste and debris in biohazard bags. DO NOT autoclave.

11. Soak equipment used in 1 % sodium hypochlorite for at least 20 min and wash thoroughly with water.
12. Remember to document about the incident mentioning detailed information for future reference (Appendix 9).

3. Fire or Explosion

1. Call for help by shouting “FIRE” loudly when a fire is found and press the fire alarm button.
2. Activate the nearest fire alarm.
3. Notify personnel in the immediate vicinity.
4. Attend to human life in danger.
5. It is suitable to try to extinguish fire with the appropriate extinguisher when safe to do so.
6. Turn off electrical equipment, shut doors and evacuate the area by finding and follow the emergency exit signs.
7. Remember to use emergency door ONLY if you are trapped in laboratory and if exit through the anteroom is not possible.
8. The sound of the fire alarm act like a red alert. Except evacuation team every person inside must evacuate.
9. For safe evacuate, staff must use stairs. USE OF LIFTS TO BE AVOIDED AT ALL COSTS.
10. All staff members must move out of the building in a calm manner.
11. If it is not possible to get down by stairs, then wait outside in the balconies or verandas or the fireman/outside help to safe you by ladder.
12. Once at a safe place, assemble and see all members of your group are present and do not leave until your name has been called by facility manager and cleared off the attendance sheet.
13. If the fire started within your work area, document in detail and submit incident report form (Appendix 9).

4. Medical Emergencies

4A. Chemical or Biological Splash to the Eye

1. Do not be panic and immediately flush the eye with for fifteen minutes with gentle stream of water.
2. Care must be taken to avoid contamination of the opposite eye.
3. If available, use the emergency eyewash.
4. Seek for medical advice in your facility.
5. Remember to document about the incident mentioning detailed information for future reference (Appendix 9).

4B. Cuts and Abrasions and Animal bites

1. Do not panic; clean the damage area and surrounding skin immediately with antiseptic soap/solution. Keep wound under running tap water and encourage oozing of blood.
2. Get the first aid box. Take out sterile/clean cotton pad and place firmly over the wound and apply a bandage or plaster.
3. If the cut/wound size is big and bleeding, keep the victim in a lying position (in the anteroom) and raise the bleeding part higher than the other parts of the body.

4. Seek for medical advice; blood sample for lab tests and get the requisite vaccination.
5. If possible, the animal should be set aside for quarantine and laboratory testing. Since many laboratory animals may carry some disease, testing for infectious agents may be useful to determine proper treatment for the laboratory worker.
6. Remember to document about the incident mentioning detailed information for future reference (Annex).

4C. Needle stick injuries

1. Immediately expose and express the wound and encourage oozing of blood.
2. Make sure to immediately minimize the risk by cleaning the damage area by flushing the wound under running tap water for five minutes. Clean the wound and surrounding skin with antiseptic soap/solution.
3. Cover the wound with bandage and doff the laboratory PPE normally.
4. Seek for medical advice in your facility.
5. Remember to document about the incident mentioning detailed information for future reference (Appendix 9).

4D. Thermal Burns

1. Do not be panic and observe the wound. If skin is intact, dip the burned area in clean tap water.
2. Do not touch or break any burnt part or blister and do not apply any cream/ointment.
3 Seek for medical advice in your facility if necessary
4. Remember to document about the incident mentioning detailed information for future reference (Appendix 9).

4E. Serious Medical Emergencies

(The victim is unconscious due to some medical complications such as heart attack, fall and head injury, etc.)

1. Call 1122/ 115 or nearest medical facility for help.
2. Take off all PPE.
3. Move the victim into anteroom/ designated area and let him rest lying down.
4. Call the Basic Life Support (BLS) trained team.
5. Inform the Facility Manager.
6. Remember to document about the incident mentioning detailed information for future reference (Appendix 9).

4E. Exposure to a chemical

Training on the safety aspects of the chemicals being used is a must. Deal according to MSDS and have a copy of the MSDS made available to the referring medical facility where all the staff is expected to be evacuated to for treatment (see Appendix 5 for a sample MSDS document). Thorough appraisal and training of the recipient facility is also necessary.

Laboratory Evacuations

This entails that procedures and routes be clearly identified. Alternative routes to be identified and added if not already present. An organization must select a responsible individual to lead and coordinate emergency evacuation. It is important that staff must know who will coordinate and take responsibility to make decisions during emergencies. Regular drills and mock exercises with different scenarios can be practiced regularly.

Red Evacuation

1. This type requires immediate evacuation as life is at risk. Examples include high intensity explosions or fires, massive earthquakes or toxic gas release.
2. Laboratory staffs are asked to immediately evacuate the laboratory using whatever means necessary.
3. Proper procedure for containment is not maintained.
4. There is substantial risk to life.

Yellow Evacuation

1. This type of evacuation is required immediately when there is an unconscious or injured staff or there is obstructed exit preventing the staff from adhering to usual evacuation procedures.
2. Laboratory staffs are asked to immediately evacuate using modified decontamination processes.
3. Proper procedure for containment is maintained through modified evacuation processes.

Green Evacuation

1. This type of evacuation is required when a non-life-threatening event happens (i.e., alarms, smoke, cabinet failure or low intensity earthquake or chemical or biological spills).
2. Laboratory staffs are asked to secure their work (pathogens and animals), exit the laboratory using normal doffing processes, log and report incident.
3. Proper procedure containment is maintained through normal evacuation processes.

All laboratory personals are required to assemble at designated area outside the building after evacuation. Emergency response coordinator must take attendance to ensure that everyone has safely exited. It is mandatory not to re-enter the laboratory until the emergency response coordinator notifies.

Power Outages and Stand by Generators

Many vital equipment needs a continuous supply of electricity for proper functioning. This 24/7 requirement puts extra responsibility on the lab managers to provide primary and reliable secondary source of power whether internally from the same facility or outside source. The plan designates a person responsible to switch the sources and coordinate the power supply in such situations. There should be a mechanism in place to routinely check the supplies and smooth initiation and execution. Posters listing the personnel, emergency numbers and immediate measures to be taken in such situations should be placed at all critical areas of the lab.

Stand Alone Lab/ Alternate Facilities

The emergency encountered may require a temporary shift and relocation of the lab facility or some of the vital operations, as part of the continuity of operations plan. In such circumstances it is essential to move important pieces of instruments and equipment and the required consumables. Maintaining a list is necessary for the timely re-establishing of a functional unit. The alternate site has to be examined and required changes made accordingly beforehand to operationalize the equipment.

OCCUPATIONAL HEALTH PROGRAM AND MEDICAL SURVEILLANCE PROGRAM

The corner stone of any good employee health support plan is a well-organized and coherent Occupational Health Program (OHP). This program covers all aspects of occupational health including medical emergencies and its management. The OHP ensures the placement of and referral to the right individual who can respond to the medical emergencies and can manage such incidents and patients.

Within the ambit of the occupational health comes the medical surveillance. The lab director is directly responsible for ensuring a smooth medical surveillance program and hence is a lab based and lab owned program. This surveillance ensures the detection of the symptoms of the agent with which the lab is working and ensures that the individual is then guided to the medical authorities competent to deal with the situation. The problem of working with biological agents is compounded by the fact that a lot of time may be required for the symptoms to appear; hence it is imperative that vulnerability to the suspected agent is kept in mind.

This may include a thorough knowledge of the transmission routes, so that extra vigilance may be exercised if protective items fail or exposure is suspected. It however, critically, hovers on the symptomatology of the agents with which the lab is dealing. Once the symptoms develop, the individual reports for medical treatment, as outlined by the OHP, through the director of the lab. The director must be in picture of exposed personnel. The surveillance is on the outlook for detecting trends within the staff. The surveillance may be based on sentinel and stand-alone cases. Typically, it monitors for common source exposure and tries to limit the damage done both to the individual (secondary prevention) and other workers by modification/limitation of the procedures (primary prevention).

This begins with the director providing a list of essential symptoms for the agent, contact numbers for a 24/7 appraisal and guidance; and healthcare facility and person to be contacted. The monitoring of the health status is vital in this surveillance and close communication of the director with the occupational health clinic is imperative. Changes in the procedures and SOPs as well as other modifications of biosafety can only be exercised when timely feedback is ensured. The cycle closes when appropriate measures have been taken. The surveillance program also entails that periodic revision of the symptom sets is done, and the workers fully understand what is expected out of them individually that would help the co-workers collectively.

A simplified flowchart for the medical surveillance is appended below.

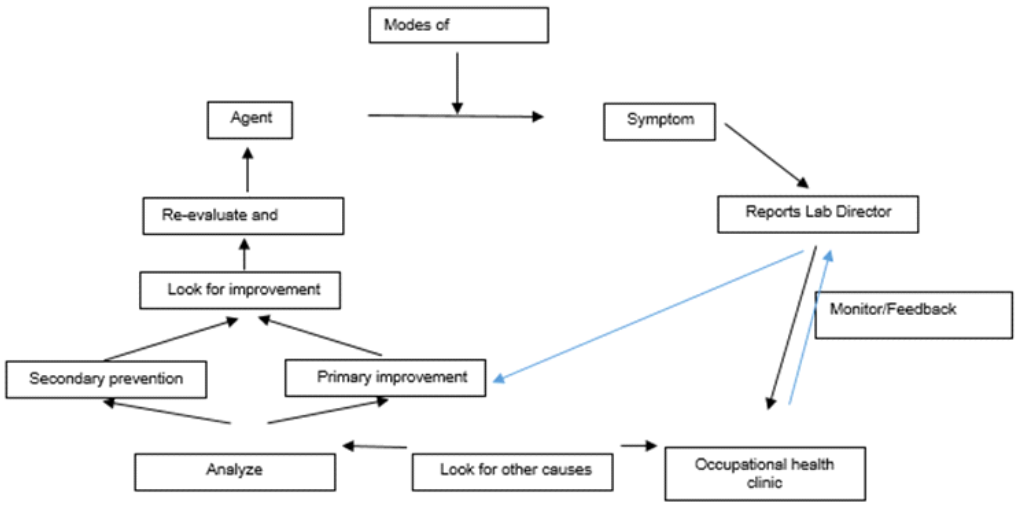


FIGURE 10-1. Flow Chart for Medical Surveillance

ACCIDENTS, INCIDENTS, NEAR MISSES AND UNDESIRED CIRCUMSTANCES

The lab must decide and train its workers and managers as to how it defines the sustained or exposure to bodily injury and harm as relates to accidents, incidents, near misses and undesired circumstances. This is pertinent in the context that different definitions exist for these events in the literature of occupational safety. Hence an agreement has to be reached before hand as to the exact definitions for these events. The problem may be aggravated when staff is rotational and not permanent. Whatever definition the organization/lab chooses, reporting has to be on that format for the purposes of record and review.

The events must be investigated thoroughly, and root causes identified to eliminate /reduce the chances of happening again. Emphasis on 'what went wrong' has to be exerted rather than 'who went wrong'. Trouble shooting with only this aspect in mind can lead to culture of safety.

Adequate remedial measures and timely actions can prevent further untoward events. A simplistic flow chart is appended below for a guide (Figure 9-2). See Appendix 9 for an Incident Reporting Form.

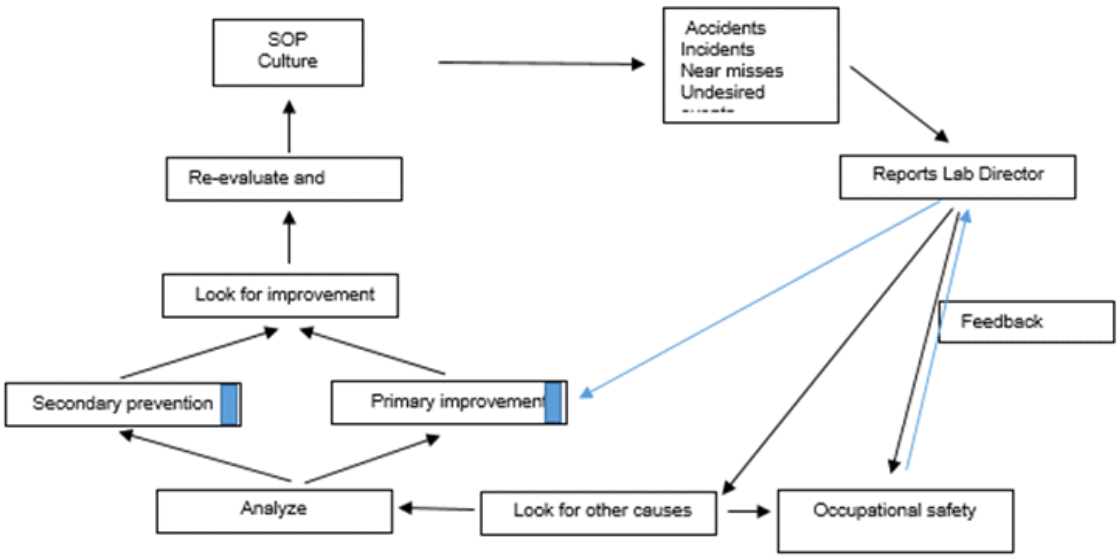


FIGURE 10-2. Flow chart for incidents/accidents

BIBLIOGRAPHY

Chemical Spill Response Procedures. Department of Environmental Health & Safety; Stony Brook University.
EPS Chemicals, Inc. MERCON Mercury Spill Kit Users' Manual: pp 12.
Genesee County Health. Annual Report 2014. Available at: http://www.co.genesee.ny.us/doc/health/2014_Annual_Reprt_GCHD.pdf.
Lab Safety Supply. 2011. BC1; 1st Ed: page 713.
Laboratory Fire Procedures, Environmental Health & Safety, Fire Safety, Oklahoma State University. Available at: http://ehs.okstate.edu/hazmat/fire-in-lab.htm.
Medical Emergency Procedure, University Library, University of Illinois at Urbana Champaign. Available at: http://www.library.illinois.edu/administration/services/policies/med_emergency.html.
Procedures to be followed in case of a laboratory fire, environmental health and safety. Columbia University. Available at: http://ehs.columbia.edu/LabFireProcedures.html.
Spill Response, Available at: http://www.safety.duke.edu/programs/SpillResponse.htm.
Standard Procedures for Mercury Spills. Available at: http://www.delval.edu/pages/environment/C1280/.
WPI Chemical Spill Response Procedure. Available at: http://www.wpi.edu/offices/safety/chemspill.html.

SECTION III:
LABORATORY OPERATIONS

Chapter 11

Preparation of Procedure Manuals

Irfan Ali Mirza, CMH Lahore Medical College

INTRODUCTION

The procedure manual offers a basis and foundation for any laboratory's quality assurance program. The primary purpose of procedure manual is to ensure uniformity while endeavoring for quality. It is like guideline or instruction book which contains a series of directions as to who is supposed to do something, when it should be done, how this is to be done, where it should be done and what the results should be. The procedure manual will be helpful when training new laboratory technologists on lab practices, documenting how analyses are performed and for troubleshooting test problems. The procedure manual should be evaluated on regular basis and amended as necessary especially when new tests are added or laboratory procedures change.

BENEFICIARIES OF PROCEDURE MANUAL

As the procedure manual serves as central and key guidebook containing details of all the procedures used in the laboratory, so it can be of use to multiple users and personnel working in the unit. The beneficiaries of this documents include laboratory managers, laboratory directors, technicians, students, support staff, new employees, trainers, and any other person performing work in the laboratory.

ADVANTAGES OF PROCEDURE MANUAL

A procedure manual provides the clear, concise guidelines for any laboratory worker regardless of the status or length of time laboratory workers may be serving. A well prepared and reputed procedure manual provides ease of access for all laboratory workers. The procedure manual identifies a contact person in the laboratory in case of any issue. An updated and constantly revised version of procedure manual meets the changing customer needs and to adapt to new environments. Precisely written procedure manual serves as foundation in which laboratory is held accountable.

REQUIREMENTS OF A PROCEDURE MANUAL

A procedure manual should have detailed account of how different samples are dealt within lab, including sample collection, processing, and analysis. The procedure manual should outline how samples should be collected, stored and transported. It should also contain the detailed instructions about the specimen to be submitted in laboratory and the way it is handled. It should also contain the elaborate instructions on shipment procedure to referral lab if required.

The detailed steps for any procedure contained in the manual should begin and end without any ambiguity. While giving detailed account of procedural steps, solid action verbs should be used so that readers know exactly what to do. It should also mention the measures to be adopted in case the test system gives any problem. The information contained in the manufacture's package inserts should be used to operate the equipment as well as for carrying out any test procedure. Any information other than contained in package insert may be incorporated in manual for the comfort of laboratory workers. All the procedures, mentioned in the manual should be approved, duly signed with date by the in-charge of laboratory / director.

The manual should contain the reference or normal test ranges where applicable and should mention the critical (imminent life threatening) lab results. It is important to know specific criteria for rejection of samples. The manual should include suitable conditions for storage and preservation to ensure specimen integrity till such time the analysis is completed. In case of revision of the manual, the laboratory must have the copy of previous procedures for specified period.

PRACTICAL INSTRUCTIONS FOR MANUAL

The scheme and lay out of a manual are dependent on the lab's needs and organization. Some of the useful tips include:

1. It is recommended to use a spiral or ringed binder to preserve the document in a lay out which can easily be appraised and updated subsequently.
2. Preferably the pages of the manual should be encased in plastic page protectors to prolong the life of the manual.
3. The manual should have numbered table of contents in the beginning for easy reference.
4. Each procedure should commence on a new page.
5. A good procedure manual utilizes a great deal of white space with clear headings and sub headings.

How a Procedure Manual should be written?

Procedure manuals should be written by keeping the current documentation and record as source material. Experts in the field should provide input into the procedure manual. In certain cases, it is advisable to watch a trained person perform the procedures and simultaneously take notes or alternatively ask the person to write down all the steps involved as well as any instructions or specific guidelines base upon experience.

Each page of the document should be titled with the procedure's name. The principle of the test or procedure can be written followed by tips or warnings. The procedures once written as initial draft must be asked to be performed by inexperienced worker or technician before making it final. This allows for clarification or changes to be made as necessary. It is always helpful to have a table of contents and glossary defining any terminology specific to a laboratory.

Table of Contents of a Laboratory Procedure Manual

Although each laboratory has different requirements and thus table of contents can vary; however, following contents can be included:

a. General Information.
   - List of basic equipment used in laboratory like microscope, slides, coverslip, water bath, incubators etc.
   - The responsibility of laboratory technicians.
   - Laboratory rules to be followed.
   - Laboratory safety rules to be practiced and followed.
   - First aid and emergency practices.
   - Labelling of laboratory specimen.
   - Cleaning and storing of the glassware.
   - Disposal of specimens.

b. Microscope use and its parts.

c. Clinical pathology procedures: like stool routine examination and urine routine examination etc. Each hematology procedure has to be written in detail with principle, requirements of test procedure, procedure steps, interpretation and requisite reference ranges/values.

d. Hematology procedures: Each procedure has to be written in detail with principle, requirements of test procedure, procedure steps, interpretation and reference values.

e. Microbiology procedures: Each procedure has to be written in detail with principle, requirements of test procedure, procedure steps, and interpretation. The different samples dealt in the laboratory must be mentioned with the media requirements, incubation details, the common biochemical identification methods and antimicrobial susceptibility according to (Clinical & Laboratory Standards Institute (CLSI) guidelines.

f. Chemical pathology procedures: Each procedure has to be written in detail with principle, requirements of test procedure, procedure steps, interpretation and reference ranges/values. Every test procedure e.g. urea, creatinine etc. must be written with the principle along with the equipment details.

g. Histopathology procedures. All histopathology procedures must be written in detail like specimen collection and storage, fixation, gross examination, staining procedures and immunohistochemical markers and procedures.

h. Immunology & Virology procedures: Each procedure pertaining to immunology and virology has to be written in detail with principle, requirements of test procedure, procedure steps, interpretation and pertinent reference values.

i. Quality Control & Assurance: This is the most important section ensuring precision and reproducibility of all the procedures.

Outline the Laboratory Rules

It is always advisable to outline the laboratory rules at the beginning of the document for better appreciation of the reader. Some of the rules for the general section of the manual include:

- Follow the recommended and proper test procedures.
- Never adopt or use shortcuts.
- Always consult and refer the manual for any procedural query.
- If you do not know something it is always better to speak out.
- In case of any doubt it is better to ask for expert's advice.

- Always reconfirm any irregular or unexpected results; it is advisable to repeat the test.
- Maintain the test equipment all the time.
- Learn to work quickly and accurately.
- Always keep your work place clean and tidy.
- Laboratory results are confidential, so do not disclose them to unauthorized personnel.
- Maintain the record registers properly.
- While using the equipment and reagents the manufacturer's instructions should be stringently followed.
- All the reagents used in laboratory must be clearly labeled.
- Whenever new reagents are prepared, the label must include the name of that reagent, date of preparing and expiry, and authenticating initials.
- The reagents and chemicals should not be used beyond the expiry dates.
- Any reagent or chemical close to expiry date must be informed to laboratory manager.

Outline the Laboratory Safety Procedures

Following laboratory safety procedures can be written in the general section of the manual:

- Mouth pipetting must be strictly prohibited.
- All the dangerous, flammable and hazardous chemicals should be labelled.
- The bottles of acids and alkalis should be kept in the lower shelves of the cupboard. The hands of the workers must be dry while handling such bottles and such bottles must be kept upright while handling.
- While adding acid to the water for any test procedure do it slowly and gradually.
- Bottom of the test tube should not be heated; the middle part should be subjected to heat shaking gently with the opening of the tube which is pointed away from the worker.
- The inflammable liquids like acetone, ethanol benzene should never be placed close to open flame.
- Whenever tuning on the burner, first light the match and then hold it close to burner and slowly turning it ON.
- The Bunsen burner or gas must be turned OFF after finishing off work and always ensured while leaving the lab.
- Used syringes and laboratory waste must be disposed of appropriately.
- The first aid practices and kits should be known to all technicians in case of any laboratory accident.
- Always wash your hands after handling the specimen and before exiting the lab.
- Eating and drinking in laboratory is strictly disallowed.

Outline the Laboratory First Aid Procedures

The laboratory workers are often exposed to many accidents involving acids, alkalis, broken glasses, needle stick injuries or electricity. For all such events the

laboratory must have the written instructions as what to do in case of any such event and whom to report. Following materials must be readily available and not kept in lock:

- Wash bottles containing normal saline.
- Adhesive bandages.
- Antiseptic like pyodine.
- Cotton wool and sterilized gauze.
- Fire extinguishers and blankets etc.

Outline the Specimen Labelling/Identification and Record

The general section of the laboratory manual should contain the instructions regarding specimen labelling and identification procedures. Different laboratory specimen which are received in the laboratory must be accompanied with request form which is duly signed by the medical officer and completed in all respect as regards patient's identification. The specimen must be numbered with unique identification number written on the request form as well as on specimen/slide/test tube. In case computerized record service is not available, the results may be entered in the registers kept in respective sections of hematology, microbiology, chemical pathology and histopathology.

Outline the Tips for Cleaning of Glassware

The general section of the manual should also contain the instructions as how to proceed with the cleaning of glassware. Following set of instructions can be useful for laboratory technician:

- It is ad visable to rinse all the tubes, beakers and other glassware in slightly warm water. The blood-stained glass tubes should not be soaked in hot water.
- The glassware may be kept in washing powder or liquid detergent added water for 2-3 hours. The inside of the test tubes must be cleaned properly with some brush.
- The soaked glassware should be removed one by one and it should be rinsed with the tap water. It must be ensured that no debris or residue is left inside the glassware.
- All the washed glassware should then be properly dried by placing it on the rack or inverted. Alternatively, hot air oven can also be used to dry the glass ware by keeping the temperature around 60°C.
- In case of automated washers, instructional manual should be followed.

Outline Instructions on Disposal of Waste

The general section of the manual must outline instructions regarding disposal of waste. The following instructions can be helpful in this regard:

- The waste needs to be segregated as infectious and non-infectious in different sections of the laboratory.
- The infectious waste needs to be collected preferably in red colored containers with a biohazard sign, while the non-infectious waste needs to be collected in either yellow colored bags.

- Sharps should be collected in hard boxes.
- The disposal of infectious waste needs autoclaving followed by incineration or shredding and burying.
- The noninfectious waste needs to be disposed of as per protocol of the hospital.

Samples of Common Procedures to be incorporated in Procedure Manual

Appendix 11 contains common procedures of different sections of lab which can be incorporated in the procedure manual. These have been outlined for guidance only. The laboratory should be able to write all the procedures pertaining to their area section wise.

BIBLIOGRAPHY

Anderson, C. What is the purpose of procedure manual? Available at: https://www.bizmanualz.com/improve-business-processes/what-is-the-purpose-of-a-procedure-manual.html.

Erren, K. How to write procedure manual? Available at: http://www.ehow.com/how_5245583_write-procedure-manual.html.

Guide to writing policy and procedure documents. Available at: https://policy.ucsc.edu/resources/images/GuidetoWritingPolicy.pdf.

NCCLS Document GP2-A3. Clinical Laboratory Technical Procedure Manuals, 3rd ed.; The New Poor Man's (Person's) Guide to the Regulations. Laessig and Ehrmeyer.

Policy and procedure writing guide. VCU policy library. Available at: https://policy.vcu.edu/sites/.../Guide%20to%20Writing%20Effective%20Policy.pdf.

Stanford Nanofabrication Facility. Laboratory Manual Part 1. Policies and Procedures.

Chapter 12

Laboratory Waste Management

M. Asghar Javaid, Nishtar Medical College, Multan; Affan Shaikh, U.S.

All the workers in scientific or clinical laboratories are exposed to various hazards; working with hazardous biologicals and chemicals is a routine practice. Most of the biomedical wastes in hospitals are produced in the laboratories. Not only it is costly to dispose biomedical wastes but is also associated with the risk of various infections like Hepatitis B, Hepatitis C and HIV.

The substances having features such as reactive, corrosive, flammable, radioactive, poisonous, toxic, infectious or carcinogenic are known hazardous materials having potential risks to humans as well as environment. As tested material hazards are unknown, the use of "universal precautions" is necessary. It is the duty of trained laboratory personnel and research workers to safely and correctly dispose of all wastes produced during their work.

All laboratories should have a **Waste Management Plan** and this plan must be stringently followed by laboratory personnel. It is the duty of laboratory managers to train new employees on appropriate disposal of all medical wastes and ensure that the plan is being followed. Laboratory Manager/Safety Officer minimizes risk exposure by designing and conducting laboratory work according to safety policies. Medical waste disposal providers should also train managers and staff for better compliance. Laboratory workers should be familiar with protocols to follow in the event of an exposure or spill (see Chapter 10 for handling spills).

TYPES OF WASTES

Hazardous Waste: Waste generated through direct contact with the specimen or product containing or suspected to contain hazardous material. Hazardous materials may exhibit one or more of the following characteristics: ignitable, corrosive, reactive, and toxic constituents that have been shown to be harmful to human health or the environment. Hazardous waste can be: injectables, raw material, expired reference/standard material, chemicals/reagents/solvents, microbial cultures, culture media, silica gel, animal carcasses, sharps (glass implements, needles, syringes, blades etc.), used membrane filters, used absorbent pads, used disposable gloves, used tissue papers, used cotton plugs, used filters, and contaminated muslin cloth among others.

Hazardous waste that contains infectious agents is called biohazardous waste. It includes:

- Medical waste: Medical waste means any solid waste generated during process of providing medical services.
- Biological waste (Infectious & Non-Infectious): Cultures, plates, media and other

liquid or solid materials generated by laboratories, having contact with microorganisms in body fluids and clinical materials.

- Infectious waste: Any waste which contains or suspected to contain any infectious material or waste generated by coming in contact with body or fluids of an infected person.
- Pathological waste: Organs, tissues, body parts or fluids are known as pathological waste. A sub-group of pathological waste is anatomical waste which includes recognizable infected or non-infected human body parts. It should always be considered potential infectious waste.
- Radioactive waste: Liquids, gas and solids contaminated with radio-nuclides having toxic effect is called radioactive waste. Radioactive waste is of two types: low-level waste is produced in medical and research centers while high-level waste at nuclear reactors.
- Chemical waste: Many materials such as discarded commercial chemical products, process wastes, and waste water are included in chemical waste. Products used for disinfection procedures and batteries are also considered chemical waste.
- Cytotoxic waste: A contaminated substance containing material which is genotoxic (teratogenic, carcinogenic, mutagenic) to cells or on reproduction.
- Non-hazardous waste: Waste is called non-hazardous when it has no direct contact with the contaminated specimen or product. Packing material, PVC, aluminium foil, unused glass bottles, paper, card board, are few examples. Office supplies, packing boxes, or office supplies used in the laboratory are also included.

IDENTIFYING HAZARDOUS WASTES

By addition of contaminants a nonhazardous material may become a hazardous material. It is very important to separate hazardous and nonhazardous waste. Material Safety Data Sheets (MSDSs) or Safety Data Sheets (SDS) should be a source of information before purchasing a new chemical. MSDS should be available in Laboratory (see Appendix 5 for sample MSDS). If there is confusion about the composition of a waste resulting from an experimental process, laboratory workers must consult the Laboratory Supervisor or Safety Specialist.

FOUR PRIMARY WASTE DISPOSAL TECHNIQUES

There are several ways to dispose of waste, however, the appropriate method will depend on the type of waste. There may be necessary treatment steps prior to the final waste disposal. For instance, any liquid that may contain any infectious agent needs to be disinfected prior to disposal. This will prevent the accidental release of pathogens into the public sewer system. In addition, some chemicals cannot go down the drain as they may damage pipes, sewer systems or cause toxic chemicals to enter the public water supply. All laboratory workers should be aware of these issues and properly educated regarding waste treatment and disposal.

1. Liquid treatment system: Any liquid containing infectious material should be disinfected prior to disposal. Disposal should occur within the guidelines of the laboratory waste management policies.

2. Incineration: Incineration is used primarily for infectious waste including laboratory waste.
3. Shredder: This technology is replacing incinerators so as to protect the environments. The treated waste can then be buried.

The use of incineration or landfill will vary based on the laboratory's institutional practices.

WASTE MINIMIZATION

Reduction in the quantity of hazardous wastes achieved through a use of innovative or alternative procedures is called waste minimization. All hazardous waste generators should practice waste minimization as it is cost effective as well. Following activities may be included in waste minimization:

1. Substitutions of less hazardous materials (A non-hazardous or less toxic chemical can be used in place of a more hazardous chemical in a given process).
2. Treatment to reduce hazards.
3. Change in procedure to minimize generation.
4. Improvement in laboratory management practices.

WASTE PREPARATION

1. There should be no delay in waste removal; allowing buildup of waste can in itself lead to a hazardous situation.
2. Collection and segregation of waste must be according to type and degree of hazard. It is important to use proper containers or bags when collecting hazardous waste. Storage of waste containers should not be near a location where a spill can occur. The containers must be placed appropriately; never next to sinks. Toxic chemicals can enter the sewer, and emit toxic gas causing health hazard or explosion. Store waste containers in an explosion-resistant solvent cabinet. Waste bottles must not be placed in hoods. Storage containers should be kept closed and must be labeled properly. Food containers should not be used to store hazardous waste (like water bottles, juice and milk boxes, etc.).
3. Approved washable and easily disinfected PVC containers with a capacity of 40-50 liters should be used for packing of waste material.

THE LABELLING OF WASTE

Requisite "HAZARDOUS WASTE" label/symbol must be attached to the container.

1. The “Date of First Use” and the chemical composition of the waste must be written on the tag when the initial hazardous waste is placed in the container. For chemical identification, formulas and abbreviations are not allowed.
2. The physical state must be indicated as either a gas, liquid, or solid and class of hazard must be mentioned on tag.

The presence of an oxidizer, sulphide, or cyanide if present, must be written on the tag.

1. Organic waste/xylene waste like terms should not be recommended. Label these as "Used Xylene" etc.
2. If the pH is known, it is listed on the disposal tag.
3. In case of liquids, at least 2.5 cm of space must be left at the top.

The outside of the bottle is kept clean and dry with utmost care taken to not contaminate the outside of the container. Laboratory controlled waste containers must be emptied regularly.

COLOUR CODE FOR SEGREGATION OF WASTE MATERIAL

The colour coding currently in the manual is recommended by WHO, however, a hospital/lab could adopt its own coding as long as there is uniformity/harmonization within the hospital/lab. Institutional guidelines should specify the colour coding used to identify laboratory-generated waste materials. Examples:

- Yellow - Puncture proof container for Glassware/sharps.
- Black - General waste (paper and cartons etc.).
- Brown - Chemical/pharmaceutical material.
- Red - Infectious/biological material.
- Grey - Metal.
- Blue - Plastic.
- Green - Organic materials.



FIGURE 12-1. Coloured coding

Separating the Waste

- Proper separation of waste in the laboratory is mandatory for a safe workplace environment. Do not put all wastes in the same cabinet. Only chemically compatible waste can be mixed together and placed in a common container for disposal.
- Acids should not be stored with bases /organic waste/ cyanide, sulphide or arsenic compounds in the same cabinet.
- Alkali or alkali earth metals and aqueous waste should be placed.
- Powdered or reactive metals and combustible materials must be stored in different separately cabinet.

- Mercury or silver and ammonium containing compounds should not be mixed.
- Halogenated wastes should be separated from "regular" organic wastes whenever possible.
- Syringes or needles should not be put in a laboratory waste bin or controlled waste container. '
- Sharps' contaminated with biologically hazardous materials must be collected in special containers to be sent for incineration.
- Glass bottles are good general-purpose containers for liquid wastes, with the exception of hydrofluoric acid which dissolves glass and must be stored in thick plastic containers. Use only glass or polyethylene containers for waste.

INFECTIOUS WASTE

All biomedical waste MUST be kept in autoclavable RED bags bearing the biohazard symbol. The bag must be filled up to two-thirds to avoid any spillage. Infectious waste must be double bagged to avoid any outflow. Any leaking bags should be repackaged.

DISPOSAL OF WASTE

The disposal of laboratory wastes (chemical, hazardous and non-hazardous, radioactive, bio-hazardous, or unwanted materials including Universal wastes) has become more complex and expensive as regulations have become more stringent. Laboratory personnel are responsible for identifying and labelling waste generated in the laboratory and storing it safely until it is removed for disposal. Accumulation areas in laboratory can be properly managed with frequent disposal. According to hazardous waste guidelines, a waste container can be kept in a laboratory no more than three days.

MATERIALS AND EQUIPMENT

For infectious waste disposal following items are mandatory:

1. Colour coded containers for waste collection;
2. Personal protective equipment (PPE);
3. Autoclave;
4. Incinerator;
5. First aid box and spill kit.

Supervise Housekeeping Staff

Supervise housekeeping staff that collect and transport wastes for disposal. Ensure that housekeeping staff immediately seal and replace filled waste collection bags with new ones. Prevent unsupervised and unauthorized dumping of infectious or non-infectious waste in undesignated areas. Inspect the work area to identify hazards and develop actions to control them. Ensure that employees follow safe work practices.

WASTE STREAMS ASSOCIATED WITH THE LABORATORY

1. Waste material like gloves or pads mixed with blood or body fluids.
2. Chemicals like acids, alkalis, alcohols, flammables.
3. Chemotherapy waste in pharmaceuticals.

4. Radioactive substances used for testing and treatment.
5. Recyclable material including non-contaminated paper, glass, aluminium and plastics.
6. Municipal waste/Regular trash.
7. Sharps – Objects or devices having rigid corners, edges, points or protuberances capable of cutting or penetrating the skin are called sharps. These are hazardous because of the danger to cause cuts and punctures. These can also be contaminated with potential biohazardous material. Examples of sharps include: hypodermic needles, all syringes to which a needle can be attached (with or without the needle), scalpel/razor blades, pasture pipettes, blood vials, glass capillary tubes, needles with attached tubing, broken or unbroken glassware, such as slides and cover slips, used pipette tips in contact with an infectious agent. Used pipette tips having no contact with biohazardous agents should not be disposed in sharp container.

Chemical Waste

Collect all chemical waste in a labelled, leak proof and nonreactive brown coloured container. Avoid adherence of harmful material to the outside of container. Treat or neutralize the chemical waste (if required). Maintain disposal records in the relevant logbook accordingly.

Biological Waste

Place all biological materials or materials coming in contact with infectious source in the appropriate red coloured container. Decontaminate the material in an autoclave for an appropriate period. Maintain records in relevant logbook accordingly. It has to be sent for incineration.

Infectious Laboratory Waste

Steam autoclaving is the method of choice for decontaminating microbiology culture media, laboratory glassware, pipettes, syringes, or other small items known to be contaminated with infectious agents like HIV, HBV, HCV and other dangerous pathogens. Blood and body fluids contaminated materials are treated as infectious laboratory waste. Location of the autoclave within the laboratory minimizes storage and transport problems. Autoclave procedures should be verified routinely.

Sharps

Yellow coloured, puncture proof rigid container must be used for collection of sharps. Sharps containers typically do not need to be autoclaved prior to disposal. Once the container is three-quarters full, it must be closed and disposed of according to local requirement; presently incineration. DO NOT clip, bend, shear, or separate needles from syringes. DO NOT recap needles before disposal.

Plastic Waste

The disposal for plastic waste is determined by the nature of the contaminants. Collect the waste in blue coloured container. Incinerate the contaminated waste as required. Maintain records in relevant logbook accordingly.

Special Waste Storage

It is recommended that chlorinated solvents must be in glass containers. Unknown wastes and explosive waste must be handled on a case-by-case basis.

Mixed Waste Collection and Storage

Mixed waste is hazardous due to its constituents that may be radioactive, chemical or infectious. Handling of mixed waste in the laboratory must be conducted in accordance with all relevant radiation safety procedures and hazardous waste procedures.

Waste Bottles

Loosely cap organic waste bottles to avoid a pressure build up in the bottle. Funnel should not be left in the waste bottle. Placing of the funnel to incompatible waste bottle can cause fire or explosion.

Empty Containers

Write “Empty” on the chemical container that is completely emptied. Do not put containers in the trash with hazardous symbol. Some empty containers cannot be thrown away in the normal trash due to toxicity of residual chemicals.

Ethidium Bromide Gel

Ethidium bromide (EtBr) is an intercalating agent commonly used as a fluorescent tag (nucleic acid stain) in molecular biology laboratories for techniques such as agarose gel electrophoresis. EtBr gel should be collected in leak proof containers and affixed with a hazardous waste label or tag. Do NOT use biohazard bags.

Debris

Contaminated towels, gloves and shelf paper used for cleaning spills or leaks of hazardous material, should be bagged and labelled as hazardous waste. Debris in contact with the outside of the container and with no visible contamination can be discarded in the regular trash.

Municipal Laboratory Waste Disposal

Municipal lab waste includes office supplies, packing materials, other disposal lab materials and boxes that were received or used in a laboratory. These items can go into the normal trash or recycle bin. Confidential patient record requires appropriate special disposal like shredding.

AUTOCLAVING

Autoclaving is required for solid biological waste for 30 minutes at 15psi and 121°C. Autoclave tape strip is applied on the bag before beginning the sterilization cycle. Following the autoclave process, the material is considered non-biohazardous waste.

INCINERATION

The treatment process that involves the combustion of waste material at very high temperatures (1200-1400°F) is known as incineration. Incineration is one of the common

disposal methods for laboratory wastes. Incineration and other high-temperature waste treatment systems are known as "thermal treatment."

SHREDDING

In order to prevent spread of any infectious material, the autoclaved medical wastes are shredded to small pieces before being buried. Only disinfected waste should be used in a shredder. New shredders utilize combination of an autoclave or a microwave with the shredder. The waste is put into a hopper made of revolving blades/shafts that cut the waste into small pieces. These pass through a mesh and are collected at the bottom. Larger particles retained on the mesh are once again passed through the cutters.

PPE

Wear lab clothing that protects street clothing, such as a fully fastened lab coat or a disposable jumpsuit, when particularly hazardous substances (PHS) are being used. Do not wear laboratory clothing used while manipulating PHS outside the laboratory area. Lab coats are the most commonly used protection in different types of labs. Lab coats must be regularly washed. Coats used inside the labs must not be worn outside. Similarly, female employees must use separate head covers inside and outside; disposable head covers are a better choice while working in the lab.

PPE is designed to protect different parts of the body, i.e., eyes, head, face, hands, feet, and ears and use as an integral part of infection control and prevention measures and protect the workers from exposure to blood, body fluids, and other potentially infectious materials. It must be discarded as infectious waste in the biomedical labs. Discard disposable gloves after each use.

WASTE MANAGEMENT: EVERYONE'S RESPONSIBILITY

Good waste management depends on a dedicated Waste Management Committee (WNC) and Team. The Medical Supervisor of the hospital must constitute a Waste Management Team that should monitor all the processes involved. It must comprise of all relevant representation; following is suggested:

1. A Senior Officer from relevant specialty, who shall be the Chairman;
2. Heads of all hospital departments;
3. Infection Control Officer;
4. Microbiologist;
5. Chief Pharmacist;
6. Senior Matron/Nurse;
7. Representative from Administration;
8. Hospital Engineer.

Waste Management Team

The Waste Management Team is a sub component WMC and must have a microbiologist as the main member. The team is responsible for preparation of **waste management policy** which must be reviewed periodically. It shall be responsible for the preparation, proper planning, critical monitoring, periodic review, revision or updating, coordinating and controlling disposal operations, and implementation of the waste management plan and better administration.

Staff Training

Proper training must be imparted to all staff on first aid procedures. Workers should be trained on techniques to prepare and pack safely. They must know how to protect themselves from hazards of waste. SOP on waste disposal should be placed appropriately so as the lab staff is aware. Newly appointed staff members should be supervised in training.

RESPONSIBILITIES FOR WASTE MANAGEMENT

All Healthcare Workers

All healthcare workers have the following obligations:

1. Use of adequate PPE and clothing as noted.
2. Waste bags should be sealed properly and held away from face.
3. Report sharps injuries immediately to manager and ensure medical advice.
4. Any incident involving spillage of the contents of a biohazard or infectious waste bag should be recorded/reported to the manager and Occupational Safety Office.

THE HOSPITAL MUST PROVIDE

1. Facilities for hand washing, changing, storage and laundering of contaminated clothing.
2. Adequate PPE.
3. Adequate training for all staff in handling clinical and non-clinical waste.
4. Suitable transport, storage and disposal facilities for clinical waste.
5. Vaccinations of laboratory personnel, as appropriate to the potential exposures.

Contractors for Waste Disposal

Waste management is rapidly increasing problem and a complex issue. In Pakistan hospitals produce more than 250,000 tons of waste per year. Presently, there is scarcity of waste management facilities like other developing countries. However, the gap is being filled by private vendors who are hired by the hospitals on contract basis.

The Punjab Government is outsourcing to waste management companies in different cities like in Multan, Faisalabad, Gujranwala, Bahawalpur and Sialkot for swift and effective disposal. Previously, two waste management companies were given contracts in Rawalpindi and Lahore.

In any case legislations need to monitor such events; proper implementation of rules and regulations are mandatory. All waste disposal need to be verified through existing standards.

BIBLIOGRAPHY

Safe health-care waste management: Policy paper. WHO. Available at: https://www.who.int/water_sanitation_health/facilities/waste/en/hcwmpolicye.pdf?ua=1.

Management of quality services: Waste management. Available at: https://www.who.int/management/quality/Waste/en/index1.html.

Hospital Waste Management Rules, 2005. SRO 1013(1)/2005. Ministry of Environment. Government of Pakistan. Available at: http://environment.gov.pk/images/rules/rHWMRules2005.PDF.

Hazardous Substances Rules, 2003. Available at: http://environment.gov.pk/images/rules/HAZRU03.PDF.

Infection Control Management Policy 2011. Available at: http://www.healthkp.gov.pk/wp-content/uploads/2017/10/Vol-12-Hospital-Administrators_Final.pdf.

Chapter 13

Networking, Data Sharing and Communication

Muhammad Usman, Shifa International Hospital, Islamabad;
Affan Shaikh, U.S.

Components of healthcare system in public and private setups are basic health units, small to medium hospitals, tertiary care hospitals, centers providing special care, pharmacies, public health services, laboratories, and outdoor clinics. These setups are inter-related and connected with healthcare authorities at various levels to form a network. Consequently, there is flow of information among these setups, mostly in form of referrals of different types. Typically, in healthcare settings large volumes of patient related data are generated, which includes:

- Patients' clinical information;
- Medication data;
- Laboratory reports;
- Radiology reports;
- Statistical data such as census in hospital or unit;
- Morbidity and mortality record;

Pathology services of different types relate to various levels of these setups for providing diagnostic testing, resulting in flow of data to these setups. This data helps in diagnosis, management and prevention of diseases. Therefore, laboratory services are important component of this system.

LABORATORY NETWORKING

In Pakistan, medical or clinical laboratories are broadly divided in two types; private and public. In public laboratories there is usually a tiered system, in which labs work under local health authorities or directly under the provincial or national level. Private labs use channels of communication with local health authorities and sometimes directly to national and provincial authorities. Some private labs have their own network of small labs for routine testing and specimen collection points in different cities.

Pathology services can have a much broader scope as patients' samples can be referred from remote cities or field settings for specialized testing, which may not be available locally. Therefore, pathology services network is generally much wider and beyond local network. For data sharing and reporting in this network communication system with clients must be efficient. National reference laboratories for polio, measles, influenza, and tuberculosis have a much broader role and receive test samples from all across the country.

Some countries have central disease data repository or a similar database, where labs share data of priority diseases regularly. The data is used in estimation of disease

burden and trends. It is also used in predictive infectious disease modeling with the help of an application EpiModel, which is used for responding in a timely manner to prevent and control diseases.

LABORATORY DATA SHARING

Laboratory data related to disease surveillance needs to be communicated to other departments, authorities, or organizations for making informed decisions to deliver better healthcare services. This data must be accurate for analysis to provide meaningful outcomes. Integration of laboratory data into a surveillance system increases the sensitivity and positive predictive value of surveillance system because these rely on laboratory confirmation of the cases, resulting in early response to manage outbreaks. Sharing of this data can play a crucial role for better outcomes in human and animal health, and environment under one health concept.

World Health Organization is helping developing countries through integrated disease surveillance programs for emergency preparedness and response. In these programs surveillance activities in a country have a common goal of providing community service for control and prevention of diseases. These programs are based on gathering and analyzing only relevant information. Healthcare sector, both public or private, constitutes the front line of this system. Epidemiology, laboratory support, and communication are the key elements of integrated disease surveillance system.

Data in a pathology lab is generated from testing on samples. Individual test reports are used for diagnosis or management of the patient. Individual test reports of public health importance are also shared with healthcare authorities. A list of notifiable infections is usually published by the healthcare authorities. This list is regularly updated to include emerging threats. Some microbiology reports are shared with infection control team to take preventive measures for infections with multi drug resistant organisms, tuberculosis, and influenza.

Other type of data is cumulative and summary reports. These types of reports are generally used for improving quality of service, study trends, research, and infection prevention and control. This type of data is shared at departmental, organizational, local, provincial, national or international level, depending on the type of data and purpose of the study.

Antibiogram is a type of cumulative report prepared by a microbiology laboratory to guide the clinicians regarding selection of empiric antimicrobials, and also helps in understanding trends in antimicrobial resistance. The laboratory must provide this report at least annually. Research data sharing in form of a publication must have approval from institutional review board. This type of data is usually available nationally or internationally.

Laboratory data sharing is done either manually or electronically. Prior to the availability of electronic computers, manual data sharing was a cumbersome process, as it was recorded manually and shared by mail or communicated via telephone. Mail system would take long time to reach its destination. Telephonic communication with help of fax was faster than mail as data could be immediately transferred to the recipient, but data re-compiling to generate reports was again a cumbersome task. With the advent of programmable electronic computers, the process of data collection and sharing has

become extremely efficient. Data sharing locally, remotely, anywhere in the world, can now be done almost instantaneous due to the availability of internet.

In Pakistan, Laboratory Information Software (LIS) is used by the labs, mostly in the major cities. In the private sector much better systems exist in the larger set-ups. LIS has major advantages over paper-based system. Most laboratories in Pakistan use manual paper based system. The advantages of LIS include online reporting, quick delivery of reports, uniformity in reporting, and generating cumulative or summary reports in short time. All these advantage help in efficient sharing of laboratory data.

Data sharing mechanisms are still fragmented in Pakistan. Data sharing for vertical disease control programs for tuberculosis, HIV, hepatitis and influenza has been done manually and now being transferred to District health information system (DHIS). In Punjab province, Dengue control program has better data sharing mechanism in which labs report dengue cases through an internet-based dashboard.

DHIS 2 is being used in 60 developing countries. It is JAVA based, highly customizable and flexible, and works online and offline on multiple platforms like PC's, notebooks and mobile devices. DHIS 2 has data sharing, analysis and mapping capabilities. It also has an option for defining data communication levels. Systems like DHIS 2 can easily be integrated in laboratories for quick communication of relevant data to various levels. This system is now being incorporated at **National Institute of Health** (NIH), Islamabad, which is responsible for public health surveillance of the country. A central data hub is being established to cater the needs of the country. This system is expected to be functional during the current year.

Field laboratory testing is required in various situations like outbreaks or chemical, nuclear or biological event of public health concern, or disasters like floods and earthquakes. DHIS 2 can also be applied in remote areas and field conditions as it is also compatible with cellular mobile devices. In certain situations, satellite communication, which has a very wide coverage, can also be used.

REPORTING OF COMMUNICABLE INFECTIONS

In some outbreak like situations, like viral hemorrhagic fevers, public becomes concerned and electronic media handling becomes a challenge for healthcare authorities. In such situations, laboratory provides the most important information of confirmatory diagnosis. At times the media personnel may directly approach a laboratory; any incorrect information shared can aggravate the volatile situation. In case laboratories get involved in such a situation, extreme care should be exercised in releasing verified information only. Such situations should preferably be handled by public health authorities that may designate a trained spokesperson for this purpose.

Laboratories are often involved in confirmatory diagnosis of communicable infections like influenza, Crimean-Congo hemorrhagic fever, measles, HIV and tuberculosis. Results of these infections must be communicated telephonically to the clinical team and infection control team to minimize risk to other patients, healthcare workers or public. Similarly, patients infected or colonized with multidrug resistant organisms must be reported to infection control team for isolation and contact precautions. Public health or other labs have to perform important function of communicating and advising relevant healthcare authorities regarding emerging threats

so that they are prepared to minimize risk of infection transmission to community, patients and healthcare workers.

In Pakistan, overall situation of labs networking, data sharing, and communication is not uniform across the country. Some setups are relatively well developed in both private and public sectors. Various cost effective and practical options are available to improve less developed setups. Most important measure would be to increase the awareness at all levels. These setups can be encouraged to acquire inexpensive hardware available in the country. Software like LIS, DHIS and EpiModel applied in these setups can bring a significant transformation within a short period.

BIBLIOGRAPHY

Aga Khan University Hospital, Clinical Laboratory. Available at: https://hospitals.aku.edu/pakistan/medical-and-diagnostics/clinical-labs/Pages/default.aspx.

An integrated approach to communicable disease surveillance. Weekly Epidemiological Record 2000; 1 (75): 1-8. Available at: http://who.int/docstore/wer/pdf/2000/wer7501.pdf?ua=1.

Dengue Activity Tracking System, Punjab Information Technology Board, Government of the Punjab. Available at: https://www.pitb.gov.pk/dats

District Health Information System. Available at: http://dhis.cres.pk/.

District Health Information System. Available at: http://www.dhiskp.gov.pk/.

District Health Information System (DHIS) Program. Health Department, Government of Punjab. Available at: http://health.punjab.gov.pk/DHIS.

DHIS 2. Available at: https://www.dhis2.org/.

EpiModel, Mathematical Modeling of Infectious Disease. Available at: http://www.epimodel.org.

One Health. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/onehealth/index.html.

Shaukat Khanum Memorial Cancer Hospital and Research Centre. Available at: https://shaukatkhanum.org.pk/contact-us/laboratory-collection-centres/.

WHO Integrated Disease Surveillance Programme, 2018. Available at: http://www.who.int/csr/labepidemiology/projects/surveillance/en/.

Chapter 14

Laboratory Information Management

Muhammad Usman, Shifa International Hospital, Islamabad;
Affan Shaikh, U.S.

INTRODUCTION

In diagnostic laboratories valuable information is generated from scientific testing related to samples. This information comprises of important data that can be used to improve efficiency of the laboratory processes as well as add to the national data pool. Information management system refers to processes that facilitate the collection, storage, organization, retrieval and analysis of data from various sources. A computerized system for laboratory data is often called a laboratory information management system and is referred to by the acronym LIMS or LIS.

Use of computers has transformed information management in today's world, increasing the efficiency of information utilization. Healthcare systems generate a huge volume of information, which, if utilized efficiently can ensure improved patients' outcomes. In healthcare systems, information management systems are used for electronic medical records of patients, radiology, pharmacy services, finance and accounts, inventory management and the laboratory. Computer based lab information systems are replacing manual systems due to their ability to handle data in a highly efficient manner. Manual systems are used in resource limited settings in developing world countries. Whatever technology is employed in a clinical laboratory; information management is an essential component of a quality management.

In any laboratory incoming and outgoing information is related to human, veterinary or environmental samples. This data is recorded manually on paper or electronically with the help of computing devices and equipment. In a hybrid system incoming and outgoing information is usually computerized, whereas most of the information related to specimen processing is manually recorded in form of logs or worksheets. In this chapter, we will present unique elements of laboratory information system, describe the prevalence, advantages and disadvantages of manual reporting systems and laboratory information systems, as well as provide risk mitigation strategies and methods for transforming from a manual reporting system to a laboratory information system.

ELEMENTS OF LAB INFORMATION SYSTEM

Successful design and implementation of a laboratory information system must include a number of important elements.

Unique identifiers for patients and samples

A unique patient identifier is an essential tool for handling information in a laboratory. Patient particulars include name, sex, age, date and time, and most importantly a patient's unique identification code. This is important as any duplication of a unique identification code can lead to major errors. Whatever mechanism is used for patient identification; duplication must be avoided. Examples of patient identifiers include:

- Patient registration or record number generated at a healthcare setting;
- Patients name, age or date of birth, sex;
- Relationship for dependent parents, children and spouse, in case of newborn infant's father or mother name;
- National identity card or passport number;
- Rank or designation;
- Identity number by the employer.

A patient can have orders for several tests for which a unique specimen or test identification number or code is allotted for every test ordered. Usually specimen identification codes are linked with patients' unique identification code. A minimum of two sample identifiers must be used throughout the process of testing in lab.

A unique patient identification code is usually generated for a patient at the time of first visit to a hospital or laboratory. This unique patient identification code is used for all the tests ordered in the laboratory. Unique sample identifiers of the patients' samples help in tracking the samples throughout the laboratory.

The full identification code must be used throughout the laboratory to avoid any clerical errors. This unique code must be used on the request forms, the laboratory registers worksheets, and the log sheets. Depending on the type of the test, these sample identifiers must clearly identify sample related containers, tissue blocks, test tubes, aliquots, slides, plates, kits, cards, culture media, etc.

Standardized requisition forms

Laboratory tests advised by physicians are followed by generating a requisition request from the clinic, unit, ward, or specimen collection point. The requisition forms are filled with all the relevant information in both manual and electronic systems. Preferably, the forms should be completed at the time of specimen collection. These forms must be kept simple and easy to record the required information in minimum possible time. The laboratories must establish a good communication system with the clinical staff to clarify any confusion or incomplete information. The form should be filled in completely, indicating all information that needs to be provided when ordering and submitting a test request. In case the request form is incomplete, communication with the requestor is needed to try to secure the needed information. In some circumstances reporting of tests that are not urgent may be delayed until the form is completed. Example of a standard requisition form is given in Fig 13-1.

Laboratory Test Requisition Form - Chemical Pathology

Medical Record Number:
Name, Age and Gender:
Unit / Ward:
Date/Time:
Test(s) required:
1.
2.
3.
4.

Diagnosis & Clinical Notes:

Physician's Name, Designation & Stamp

FIGURE 14-1. Lab test requisition form

Laboratory data records

Laboratory data can be recorded manually or electronically. Examples of manual records include:

- Logbooks and log sheets;
- Ledgers;
- Preventive maintenance records;
- Quality control logs;
- Proficiency testing reports;
- Patient reports;
- Audit reports;
- Error reports;
- Incident reports; and
- User surveys and customer feedback.

Laboratory records are permanent once finalized. However, a physician may request the lab to repeat the test on the basis of a result not correlating clinically or requesting some additional testing. In such circumstances either an addendum report is issued, or changes and corrections made to original report are clearly mentioned. Laboratory staff documenting or recording any data must carefully complete and secure the recorded information, as it is useful in sample tracking, investigating laboratory errors and doing root cause analysis.

Sample receiving in a laboratory is an important pre-analytical process to ensure that all the tests requested have been received in the laboratory. In manual systems all samples received in the laboratory are documented in a ledger or log sheet. Samples not

received in lab are difficult to track in these systems. In electronic system it is much easier to generate computerized list of samples not received in lab.

PROCEDURE TO ASSURE ACCURACY OF DATA RECORDING, REPORTING AND COMMUNICATION

In diagnostic laboratories log sheets are used for recording lab data, e.g. compiling test results. Patient identifiers required in these sheets are copied from requisition slips or forms. These results from these sheets are further transcribed or copied to other log sheets, worksheets, preliminary or final reports. During these processes, transcription errors can occur. These errors can be minimized by re-checking, preferably by someone else. Many lab tests have results in form of numerical or categorical values. Examples of numerical data includes quantitative chemical analysis on blood samples for glucose, liver function tests, and thyroid profile. Categorical data examples are qualitative attributes like positive, negative or borderline for rapid immuno-chromatography tests used for malaria, dengue etc. Data entry errors for these tests can be minimized if the LIS has mandatory double entry to enter the result twice or thrice, generating an alert if the entries do not match. Another type of data in lab reports is descriptive text in form of opinion or comments, e.g. histopathology reports. In such reports, transcription, spelling or grammatical errors can occur. Therefor these are rechecked for such types of errors.

Laboratory reports are designed to clearly and effectively communicate the results to the clients. Therefore, these reports must incorporate all the relevant information including:

- Name of the laboratory with address and contact number;
- Unique patient identifier code;
- Unique specimen identifier code;
- Name and address of requestor;
- Location where specimen is collected;
- Date and time of collection;
- Test requested and type of specimen;
- Date and time of receipt in laboratory;
- Date and time of reporting;
- Reference ranges with units, where required;
- Opinion, where applicable, e.g. in histopathology reports;
- Comments may include following type of information:
    - Telephonic communication details for panic or critical results;
    - Interpretation of results;
    - Testing methodology or its limitations;
    - Specimen quality;
    - Reason for rejection;
    - Reason for delay in reporting;

- Addendum or modification to the final report;
- References pertaining to the test.

- Verifying person signature or identity.

Laboratories must also be aware of any relevant certification or accreditation programs that they are pursuing and include any additional requirements in their reports. For example, the Joint Commission accreditation requires the laboratory to have a policy for panic or critical reports. These results must be communicated to the appropriate persons defined in policy and the communication details are recorded in patients' reports. Telephonically communicated information must include the following information:

- Caller's name and initials;
- Number called;
- Date and time of call;
- Name and designation of call receiving person;
- Panic value or results.

Read back of the report by the person noting the report minimizes communication related errors. Laboratories must have a policy for turnaround time for all the tests. Any delay in reporting must be recorded along with the reason for delay. Unnecessary delay in reporting must be avoided. In LIS, the reports are available to the clients as soon as they are verified by the lab staff. In manual reporting system the reports are dispatched to the relevant unit or department or collected by the patients themselves. Clinically significant results must be communicated to the clinical staff as it may take a long time for the reports to reach the clinic, unit or department.

INFORMATION SECURITY, STORAGE AND CONFIDENTIALITY

Laboratories must have a policy for information storage and archiving. Digital records are space efficient and can be kept for a very long time of several decades or more as huge data can be stored on physical fixed or removable disk drives. Manual records are quite difficult to store because they occupy a lot of physical space. Therefore, the policy must specify the duration of storage of different types of documents and ledgers. The records must be kept in an organized, safe and secure manner for as long as needed. The record must be traceable throughout all processes from test request to reporting, including any quality control results.

Information loss can adversely affect pathology services; therefore, measures must be taken, and policies enacted in order to secure laboratory data. In manual systems information loss may occur due to fire especially due to short-circuiting, rodents and pests (termite), water spills from rain water or leaking pipelines, humidity, or disasters like floods and earthquake.

Manual records must be archived in an organized manner, avoiding clutter, so that the records can be easily retrieved. The records must be secured in a designed area, preferably a separate room with proper electricity connections. The area must be regularly inspected to identify and address any damage to records.

Computerized system though easy to operate are not very secure. These systems have several vulnerabilities like:

- Cyber-attacks like phishing, spyware and brute force;
- Viruses and Trojans;
- Malware;
- System and application bugs.

All the above can compromise security of system and needs regular maintenance by IT professionals. The above threats attack vulnerable systems from internet or through removable storage devices. A recent phishing cyber-attack adversely affected hundreds of thousands of computers in different countries, including National Health Services in UK. To secure computers from these vulnerabilities it is essential to use an effective firewall, internet security and antivirus software. System and application related issues can usually be resolved by regular updates. The users must understand these vulnerabilities and try to avoid visiting insecure websites and clicking suspicious links in emails.

Clinical laboratories generate a lot of information related to patients. It is the prime responsibility of laboratory staff to ensure that patient related information is available only to individuals authorized to receive such information. Staff working in lab must be educated regarding patient privacy and confidentiality. For laboratory personnel it is very easy to view or print patients' reports, results, or other clinical information. Such reports must be handed over, emailed, or faxed to relevant persons only. For any suspicious situations the matter must be referred to a Lab Manager or Pathologist. Urgent lab reports must preferably be communicated directly to the treating physician or his/her team.

MANUAL PAPER-BASED SYSTEMS

Laboratories in developing countries, having limited resources, may require that a laboratory use a manual, paper-based system for all its information management. Labs in resource poor settings are unlikely to switch to LIS due to higher overhead expenses and insufficient LIS expertise. Manual systems can provide satisfactory service in these settings if key elements of information system are addressed. Registers, logs, worksheets and forms are used for information management in such systems. Even laboratories with computerized system often use partially or totally handwritten worksheets. The registers, log sheets, worksheets and forms are designed in such a way to easily manage the information. The staff must be educated and encouraged to complete the records in a legible way.

Preparing statistical, cumulative or summary reports from registers and logs can be more cumbersome in a manual system as compared to a computerized system; therefore, the registers and logs must be correctly completed by the lab staff. Incomplete registers and logs are likely to generate less accurate reports.

In a manual system, patient results are handwritten or typed in a computer. The results must be carefully entered in a report and a copy of the report is kept for archiving. Laboratory results are initially compiled in log sheets or registers. This data is then transcribed to the final report; therefore, final results must be re-checked for accuracy before the report is ready for delivery. All the data records must be initialed by a technologist or technician. The documents must be regularly revised by the senior staff, supervisor or pathologist.

Storage of reports, log sheets, and registers can become a problem over long period of time. Therefore, old records must be disposed of in accordance with record retention policy. To maintain patient confidentiality document shredding is a preferred method of disposal. Manual lab records/documents must be kept at a secure place and must be produced quickly on demand. Easy information retrieval from records can be achieved by clearly indexing, coding or numbering the files, documents and registers.

COMPUTERIZED LABORATORY INFORMATION SYSTEMS (LIS)

The use of LIS systems to manage laboratory information is a standard around the world. An appropriately designed LIS brings accuracy and accessibility to the flow of samples and data in a clinical laboratory. This system has two basic requirements; hardware and software. Basic hardware includes computers and printers, networking components, a server and may be additional back-up. Software is the application used for data input, processing and gives output of lab data when required. It works in a networking environment in which computers are linked with the server. Server(s) acts as a core or center for information processing including backing up of data. Network administrators and operators make sure that all processes of information management are running smoothly. Users of the LIS are lab staff or data entry operators, and staff or clients for generating, viewing or printing reports from LIS. Final outcome of LIS is the patients' reports, cumulative reports, summary or other reports.

A basic LIS has following components:

a. Sample registration module: In this module patient's particulars are entered in the LIS and test identity codes are generated for the samples.
b. Test result data entry and verification module: This module is used for saving and verification of test result and related data.
c. Test reports viewing module: In this module test reports can be viewed on computers on intranet or internet.

Additional components which can further automate information management are:

a. Sample requisition;
b. Sample receiving;
c. Equipment interfacing;
d. Specimen tracking;
e. Data search, statistical analysis and cumulative reports.

Different options are available for acquiring LIS. Some labs prefer in-house LIS development as part of organization information management system. Usually there is an information management department, which works on different modules of information management for the hospital, including laboratory. In some settings labs purchase a commercial system and integrate it with institutional management system. Laboratories developing an in-house computer network may use Microsoft SQL or Oracle, both are freeware, for database management. Whichever system is selected; the staff needs to be trained to operate the application.

A complete computerized information system is capable of easy data entry, analysis and retrieval. LIS are costly and initially difficult to adapt by the laboratory staff but offers definite advantages over paper-based systems. A comparison of manual and computerized information system is given in Table 1.

Table 14-1: Comparison of manual information system and LIS

	Manual system	LIS
Cost	Low as the requirement are minimal e.g. paper, ledgers and stationery items	High due to hardware and software requirements
Infrastructure requirement	Documents storage area is required	Server(s), networking components, computers and printers
Human resource	Lab staff handle documentation	Transcriptionists and operators may be needed for data entry
Training	Some training needed for documentation	Training is required for operating LIS applications
Information retrieval and analysis	Difficult	Easy
Information storage capacity	Limited as records are destroyed after certain period of time, usually few years	Large and space efficient; information can be stored almost indefinitely
Security	Vulnerable to fire, water, natural disasters, rodents and termites	Vulnerable to cyber-attacks, Trojans, viruses, malware and application bugs
Errors	High rate as data entries are done manually	Low rate due to system checks

Hybrid Systems

In hybrid systems manual and computerized systems are used in combination. Labs may use any one or two of the basic LIS modules. In case, if any of LIS basic module is not available, a manual procedure is used. For example, a lab may choose to use only LIS registration module to calculate number of patients and tests received for inventory management and audit. In case LIS registration and data entry modules are used but viewing module is not available, handwritten or printed reports are released or pdf report is shared through email.

Error reduction

LIS has different modules, which are designed according to laboratory workflow and processes. LIS with built-in system checks at the time of test verification reduces the chances of errors. For example, a system will pop-up a prompt or an alert on the screen indicating that a test value falls out of certain predefined range and gives an option to proceed with verification or cancellation. LIS with tracking option can easily provide information related to errors in specimen handling or reporting. In LIS, it much easier to track reports, to know when work was finished, who performed the work, when the data was reviewed and when the report was sent. A barcode system incorporated in LIS can be very helpful in specimen receiving at different points in a lab, as only barcode sticker on specimen container needs to be scanned.

Information access and data searching

A variety of parameters can be used for data retrieval and filtering; this helps in quick access to relevant data. It is usually possible to retrieve and use large amounts of data effectively to track and analyze trends of various kinds. Data can be searched and analyzed by name, date, duration, types of specimen, location, patient or specimen identifier, and test result or analysis performed. This kind of data searching is practically impossible with paper-based systems. Most LIS have the option of viewing previous results for the same patient for comparison. This helps in reducing errors. Similarly, results for other tests of a patient can be viewed and correlated. Inconsistencies and results not correlating with other tests or clinical information can be rechecked for errors by repeating the test. Information access also helps in generating all types of reports from the stored data, e.g. detailed list of specimens received for one or more tests for daily, weekly or monthly can be generated. Customized, summary or cumulative reports can also be quickly generated.

Financial management

Most LIS have a module to manage patient billing and generating financial reports for auditing. This helps in maintaining the financial records which are easy to audit as well and ensure transparency.

Integration with sites outside the laboratory

A LIS can be connected with sites outside the laboratory for patient or client registration and viewing or printing patient reports by healthcare provider or public health official. Computers can handle data entry into a national or local laboratory databank and almost any other data application that is needed.

Interfacing with equipment

Various automatic analyzers can be interfaced with LIS. These instruments are connected with a computer running LIS. The test results from these instruments are automatically sent to LIS; therefore, minimizing the data entry errors. Most modern analyzers and instruments have built-in capabilities of interfacing.

Total Lab Automation

Total lab automation (TLA) refers to automatic sample handling, processing, quality assurance, report verification, and sample archiving. After sample collection and labeling there is minimal manual sample handling. Pneumatic transportation system helps in minimizing sample transportation related errors. LIS plays a central role in all processes of TLA as output information from the devices is managed through LIS.

Point of Care Testing (POCT)

Certain rapid tests are done at the patients' bed side for prompt information. Examples include:

- Blood glucose by glucometer
- Arterial blood gases
- Cardiac markers like troponin

These rapid tests are not as accurate as routine testing, but help in identifying any gross abnormality. The hospital pathology department carries out the necessary quality management of POCT and monitors the reporting through LIS.

BIBLIOGRAPHY

Appavu, S.I. Analysis of unique patient identifier options 1997. Available at: https://www.ncvhs.hhs.gov/wp-content/uploads/2014/08/APPAVU-508.pdf.

International Standards Organization (ISO). ISO 15189: 2007. Medical laboratories – particular requirements for quality and competence. 2nd Ed. 2007-04-15.

Laboratory Quality Management Systems Handbook - Information Management, World Health Organization, 2011. Available at: http://www.who.int/ihr/publications/lqms_en.pdf.

NHS Cyber Attack: Everything you need to know about 'biggest ransomware' offensive in history. Available at: http://www.telegraph.co.uk/news/2017/05/13/nhs-cyber-attack-everything-need-know-biggest-ransomware-offensive/.

Snyder, S.R., Favoretto, A.M., Derzon, J.H., Christenson, R., Kahn, S., et al. Effectiveness of barcoding for reducing patient specimen and laboratory testing identification errors: a laboratory medicine best practices systematic review and meta-analysis. Clin Biochem. 2012; 45(0): 988-998.

Chapter 15

Surveillance, Reporting and Referral of Specimens

Muhammad Salman, National Institute of Health, Islamabad
Ali S. Khan, University of Nebraska Medical Center, Omaha

SURVEILLANCE

Introduction

Public health surveillance is the foundation of public health practice – the source of information to drive action. More formally, public health surveillance is the systematic, ongoing collection, analysis and interpretation of data or information needed for planning, implementation, and evaluation of public health practice (WHO). Surveillance serves as an early warning system for impending public health emergencies; documents the impact of an intervention; or tracks progress towards specified goals; and monitors and clarifies the epidemiology of health problems to set priorities for public health policies and strategies.

Types of Surveillance

Surveillance can be broadly classified in two main categories: event-based surveillance and indicator-based surveillance. **Event Based Surveillance** (EBS) is mainly used for outbreak detection based on real-time or near real-time official and unofficial reports of potential disease events from a wide variety of sources including media, rumors, blogs, community members, etc. and requires verification. EBS can be used anywhere and for all public health events including those with novel agents. While the data are usually unstructured, the collection process is mostly active and carried out through a systematic framework (WHO).

Indicator Based Surveillance (IBS) is used not only for outbreak detection but also for defining disease trends, seasonality, burden and risk factors. IBS relies on reports of individual cases of disease received from healthcare providers, laboratories, and other sources. Disease-specific or syndromic data are collected according to case definitions and are compared to baseline values to determine if disease rates are higher than expected. IBS is usually done for known diseases, where health infrastructure exists, and healthcare providers or laboratories are willing to participate in public health surveillance. However, IBS may not be as timely as EBS for outbreak detection, since IBS relies on the healthcare workers' diagnosis and interpretation of syndromic data.

Both types of surveillance include collecting, monitoring, assessing, and interpreting data. However, the types of data used and the situations in which the data are used can be different. As such, both the types of surveillance complement each other. In

addition, both types of surveillance can be strongly supported by laboratory diagnostic confirmation to determine the sensitivity and predictive positive value of the surveillance system. Thus laboratories are considered an important pillar of epidemiological surveillance.

PUBLIC HEALTH TESTING

Public Health testing refers to laboratory testing of country specific priority diseases and environmental samples as decided by national or provincial authorities. As such, public health testing is the responsibility of the government. At a minimum, the testing should include the events and diseases that require notification of WHO according to the International Health Regulations (IHR, 2005). This set includes the four mandatory diseases for notification (i.e., a single case of smallpox, poliomyelitis due to wild type poliovirus, human influenza caused by a new subtype, and severe acute respiratory syndrome (SARS)), and events that may constitute a public health emergency of international concern" (PHEIC) declared by WHO from time to time. These PHEICs generally involve epidemic-prone diseases of special national or regional concern which "have demonstrated the ability to cause serious public health impact and to spread rapidly internationally." (WHO IHR)

HEALTH LABORATORY SERVICES

Health laboratory services are categorized into: 1) clinical diagnostic laboratories, which are used for clinical decision-making and may participate in public health surveillance through laboratory reporting; and 2) public health laboratories, which collaborate with many arms of the national public health system to support surveillance and outbreak detection capabilities and serve as a reference facility. Key components of public health laboratories include disease surveillance; infectious and non-communicable disease diagnosis; environmental health; food safety; biological, chemical, and radiologic-terrorism preparedness and response; and public health informatics.

LABORATORY-BASED SURVEILLANCE

Information and data collected, compiled and analyzed by laboratories include diagnostic results from patients with varied diseases and conditions. Laboratory based surveillance systems complements both event and indicator-based surveillance and provides important epidemiological information for public health actions and for evaluating prevention and control measures. Laboratory surveillance also enables crossover conclusions drawn from the analysis of the information collected by each system separately.

Laboratory based surveillance is used for a wide range of food-borne and waterborne diseases, blood-borne and arthropod-borne infections, respiratory and zoonotic diseases. Laboratory based surveillance aims to assess temporal trends in the frequency of detection of pathogens and agents under surveillance; early detection of pathogens and agents with an increased probability of spreading; confirmation of outbreaks; and strengthening other surveillance systems.

Health laboratories are essential for the healthcare delivery system. Accurate, reliable and timely laboratory testing is an essential component for effective disease

prevention and management program(s). High quality laboratory testing is essential for clinicians to make accurate diagnoses, formulate treatment plans and subsequently monitor the effectiveness of treatment regimens. It is also important to guide national policies and treatment guidelines. Improving laboratory-based surveillance is a key component of health system strengthening and is critical to the enhancement of disease prevention and control and healthcare delivery.

Through routine, specialized and research work, health laboratories generate an enormous amount of data, which may play a vital role in clinical decision making and the development of public health policy, providing evidence-based information for disease prevention and control. Therefore, laboratories have an important role in supporting surveillance needs of national public health systems. It is equally important for laboratory managers, scientists and pathologists to understand the role of the laboratory in epidemiological surveillance and principles of laboratory-based surveillance.

ROLE OF LABORATORIES IN DISEASE SURVEILLANCE

Laboratories can support public health and surveillance systems through the following core functions:

1. Generating early warning signals and alerts:

Data collected by laboratories can be best utilized if analyzed on a regular basis. If laboratories are using an automated information system or a paper based reporting system, there should be a mechanism of alert generation so that health authorities are informed in a timely manner to undertake necessary measures for early containment of diseases of public health concern.

2. Outbreak detection and confirmation:

One of the key roles of the laboratories is detection and confirmation of an etiological agent during an outbreak. While epidemiologists capture health information including incidence, prevalence, and geographical mapping of cases which helps in assessing risk factors, laboratories confirm diagnoses and improve accuracy for treatment, management and prevention efforts.

3. Detection of emerging, re-emerging and novel pathogens and agents:

Laboratories also detect novel pathogens and provide additional details based on pathogen typing through advance techniques such as genotyping, serotyping and phage-typing, etc. In case of new and emerging pathogens or agents, besides identification, the laboratory also helps develop and validate laboratory assays and also provides information aimed at patient management and treatment.

4. Monitoring disease trends and assessing impact of interventions:

Through data generated during routine and specialized testing, laboratories also assist in diseases modelling for health services planning. For endemic diseases, laboratories support monitoring trends and evaluating the success of interventions. For instance, the national and regional immunization programs can develop immunization policies and assess the impact of the immunization programs based on the rates of confirmed disease reported. Clinicians may assess the impact of treatment protocols and modify treatment regimens based on information collected by laboratories, especially trends in antimicrobial resistance. Monitoring of disease trends is useful for both infectious diseases (e.g., sexually transmitted infections (STIs), viral hemorrhagic fevers,

meningitis, malaria, food and water borne diseases, tuberculosis, HIV/AIDS) and non-communicable diseases such as diabetes, metabolic diseases, coronary artery disease, hypertension, renal disease, and neuro-muscular genetic disorders.

5. Support disease elimination or eradication programs:

Another critical role of laboratories is during the elimination phase of a disease. Diseases prioritized for eradication require a more specific laboratory confirmation test. Public health authorities rely on laboratory confirmed diagnoses, pathogen typing and identifying the origin and evolution of the pathogen in order to track and prevent further spread of the disease.

6. Referral investigations:

Public health laboratories often require the assistance of outside laboratory facilities to provide unique or unusual testing, backup service, or for routine tests, which are not being performed by the referring laboratory. Selection of the referral laboratory is based on several factors such as cost, turn-around time, proficiency, geographical location and reputation of the laboratory. While the cost of referral laboratory services may be an important consideration, the selection of a referral laboratory should be based primarily on the quality of services provided. The referring laboratory should maintain inventory of laboratories with reference testing facilities and establish linkages with such laboratories based on objective evidence of acceptable quality and responsiveness in consultation with the institutional medical or public health staff where appropriate.

7. Development of guidelines:

Laboratories should develop and disseminate guidelines related to laboratory operations especially for the pre-analytical phase of the laboratory operation which may affect the quality of laboratory testing services. Such guidelines may include collection of various biological and environmental samples, storage, packaging, shipment of samples and documentation.

8. Capacity building:

Another important function of laboratories in the public health system is capacity building of laboratory and healthcare staff on the operations of laboratories. This should be a continuous process and laboratories are encouraged to implement diagnostic stewardship programs for improving the quality of laboratory services.

9. Research:

Laboratories play a vital role in implementing research agendas through conducting prevalence studies, basic and applied research on emerging and re-emerging diseases, understanding the natural history of new disease and developing new diagnostic tools to support clinical and public health needs. Through operational and translational research, laboratories can contribute to the overall medical research agenda of public and private organizations health systems.

ELEMENTS OF LABORATORY BASED SURVEILLANCE SYSTEM

As described earlier, surveillance is the primary strategy for tracking emerging health problems in a population, allowing for early and appropriate action. Countries should therefore strengthen their capacity for early detection and identification of etiological agents that cause diseases of public health concern.

National and regional public health laboratories should be an integral partner with the public health authority to monitor disease incidence and must ensure that they have trained scientists, pathologists, technologists, technicians, statisticians and IT support persons. Such laboratories should be adequately equipped with instruments and consumables in order to produce reliable data to support disease surveillance. The information generated should be regularly shared with relevant stakeholders and national authorities for appropriate and timely decision making.

In addition, for a laboratory to successfully undertake laboratory testing responsibilities, it must make ongoing investments in acquiring consumables, supplies, media and reagents, and ensuring quality control, along with providing periodic training for personnel and conducting external quality assessment or proficiency testing.

Laboratory-based surveillance has several requirements including the following:

- Prioritization of diseases that need to be monitored, taking into account national priorities and the burden of disease in the country;
- Selection of tests to be used for confirmation of diseases at different levels based on accuracy, cost, biosafety and bio-security requirements;
- Development or updating of SOPs for the laboratory tests using standardized methods;
- Establishing or strengthening laboratory quality management systems;
- Setting up a database for collecting and sharing information with stakeholders through existing surveillance mechanisms.

ESTABLISHING LABORATORY SUPPORT FOR PUBLIC HEALTH SURVEILLANCE

Effective participation of the laboratory in surveillance requires good communication and coordination between public health authorities, epidemiologists and laboratories. Effective coordination is vital for:

- identifying diseases of public health importance and developing a list of diseases that require laboratory confirmation;
- agreement on tests to be performed, mapping of laboratory facilities including reference testing facilities;
- establishing laboratory networking for referral testing; and
- developing mechanisms for information flow and feedback for prompt and regular reporting of results.

To establish laboratory support for surveillance, roles and responsibilities of all the stakeholders should be defined while ensuring provision of sustained supplies, logistic support, guidelines and necessary documentation for laboratory operations. At the same time, laboratories have to plan, implement, supervise and monitor laboratory quality management systems, biorisk management, information systems, waste management, participation in the development of epidemic preparedness and response plans and capacity building.

Reporting

Reporting is an essential part of any surveillance system. Timely reporting of diseases or public health events by healthcare providers or laboratories ensures the

appropriate response is generated for containing the event or the disease. In Pakistan, the Ministry of National Health Services Regulations and Coordination under the umbrella of International Health Regulations (IHR) 2005 is working to develop a national notifiable disease reporting system as part of an integrated surveillance and response system backed up with legislative framework.

However, for laboratory reporting requirements, a list of prioritized diseases has been developed at the national level and may be followed. The list includes 33 diseases and is available at https://www.nih.org.pk/wp-content/uploads/2018/11/Notification-of-Priority-Diseases-in-Pakistan.pdf. In order to initiate reporting by the laboratories, the in-charge of a public (federal and provincial/regional)/ private/ military or hospital laboratory responsible for receiving an initial order to perform diagnostic tests like serologic, immunologic, microscopic, biochemical, molecular, or culture on specimens derived from a human body or an animal, or for collecting specimens for the detection of a prioritized disease, should report such information to public health authorities. Any laboratory test suggestive or diagnostic of diseases or conditions on the priority disease list should also be reported to public health authorities. The public health system depends upon notification of diseases by laboratories to monitor the health of the community and to provide the basis for preventive action and adapted response.

Notification of a reportable disease or condition via laboratory results should be made directly to the local concerned authorities preferably Executive District Officer (Health), in the district of residence of the patient. The district health authorities in turn should share the details with the provincial Department of Health (DoH) and the National Institute of Health (NIH). It is therefore important for the laboratories to know how to contact the local district health staff, which shall remain available 24/7 especially for categories of diseases requiring immediate reporting.

Notification of reportable diseases or conditions should be submitted according to time-frames agreed upon by public health authorities and laboratories. Any notification via telephone should be followed by a subsequent written report within 72 hours by facsimile, electronic data transfer or other confidential means of written communication. The reporting laboratories should share the patient's demographic profile and information related to the laboratory tests and results along with the details of the laboratory test itself.

Referral of specimens

To fully prepare for disease outbreaks, public health authorities have to prioritize laboratory networks and disease surveillance systems to improve the response capacity. However, in resource scarce countries, without a structured surveillance system supported by a tiered network of laboratories, referral of specimens is critical for timely detection and response to outbreaks and establishing a disease diagnosis. Non-standardized specimen transport mechanisms, lack of trained laboratory personnel to transport specimens, non-availability of standard specimen containers, and long turnaround time (TAT) hinder access to quality laboratory services.

Strengthening the specimen referral system is therefore vital for the healthcare delivery system. The specimen referral system can be improved through a coordinated approach involving safe transfer of a patient sample from a resource scarce laboratory or hospital to a facility with the capability to conduct the required laboratory tests and provide

timely and reliable results. It is important to maintain the safety and integrity of specimens during transportation for analysis, and accurate and reliable diagnosis. At the same time, awareness and training to prevent healthcare worker exposure to biological materials and infection cannot be overemphasized. Packaging of infectious materials for transport as per WHO guidelines must be followed to minimize the potential for damage and deterioration of the material during transportation and prevent exposures. (See Chapter 16 and Appendix 7 for more information regarding sample shipping).

Specimen referral can be built using either a centralized approach or decentralized approach. In a centralized approach, the referral sites send the specimens to a central/regional public health or clinical laboratory for routine or specialized testing. In a decentralized model, the specimen referral system should be developed within a network having a tiered structure of laboratories that carry out varying complexity of tests at each tier, with decreasing complexity of the tests performed in each tier.

Both systems have their merits and challenges; however, the ultimate aim of establishing such a system is to reduce the turnaround time in a cost-effective way while ensuring conformity to the biosafety and biosecurity requirements.

Key interventions for strengthening and monitoring a specimen referral system may include:

- Maintaining an inventory of laboratories with specialized testing capabilities
- Increasing the number of sites referring specimens for broader coverage;
- Developing sample transportation mechanisms through postal/courier services instead of using healthcare workers;
- Decreasing the time needed to transport specimens after collection;
- Ensuring availability of specimen transport containers with triple-packaging capacity;
- Adequate number of trained staff within the specimen-referral system;
- Decreasing TAT for specimen shipment and testing;
- Mapping of referral sites.

BIBLIOGRAPHY

Core Functions and Capabilities of State Public Health Laboratories. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5114a1.htm

Global Disease Detection Operations Center: Event-based Surveillance. Available at: https://www.cdc.gov/globalhealth/healthprotection/gddopscenter/how.html.

Guide for establishing laboratory-based surveillance for antimicrobial resistance. Available at: http://apps.who.int/medicinedocs/documents/s20135en/s20135en.pdf.

How Specimen Referral Systems Can Improve Global Health. Available at: https://www.aacc.org/publications/cln/cln-stat/2017/april/20/how-specimen-referral-systems-can-improve-global-health.

Improved Specimen-Referral System and Increased Access to Quality Laboratory Services in Ethiopia: The Role of the Public-Private Partnership. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4914743/.

Laboratory Reporting Guidelines for Reportable Diseases and Conditions in Florida. Available at: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/_documents/reportable-diseases/_documents/guidelines-laboratories-2014-06-26.pdf.
Public Health Surveillance. Available at: http://www.who.int/topics/public_health_surveillance/en/.
Referral Laboratories. Available at: http://www.krrrlp.ca/files/Newsletters/TQM%20Series/TQM%208%20Referral%20Laboratories.pdf.
World Health Organization. Early detection, assessment and response to acute public health events: Implementation of Early Warning and Response with a focus on Event-Based Surveillance. Available at: http://apps.who.int/iris/bitstream/10665/112667/1/WHO_HSE_GCR_LYO_2014.4_eng.pdf?ua=1.

Chapter 16

Sample Storage and Archiving

Muhammad Salman and Muhammad Masroor Alam
National Institute of Health, Islamabad

INTRODUCTION

This chapter provides guidelines for maintaining, archiving and storing potentially hazardous biological specimens or samples. The International Organization for Standardization (ISO) and Clinical and Laboratory Standards Institute (CLSI) define samples as “one or more parts taken from a system and meant for providing information on the system”. The term “specimen” very commonly used in the laboratories refers to a sample taken from the human body. However, in ISO documents, the term “primary sample”, or just “sample” is more commonly used. To avoid any confusion, the terms “sample” and “specimen” may be considered interchangeable. Another term commonly used as far as safety in the laboratory is concerned is biological hazards or biohazards, which refers to “biological substances that pose a threat to the health of living organisms including humans” and may include medical waste, such as contaminated/used laboratory consumables and instruments, samples/specimens containing microorganisms or toxin (from a biological source) with the potential of affecting human health.

The purpose of sample management through a sample inventory system ensures to safeguard the personnel, support staff, the public, and the environment in biomedical research laboratories involving potentially hazardous biological materials (such as samples suspected of having human and animal pathogens, and synthetic nucleic acids).

IMPORTANCE OF GOOD SAMPLE MANAGEMENT AND ITS ROLE IN LABORATORY QUALITY MANAGEMENT SYSTEM (LQMS)

Proper management of samples in all phases of laboratory operations is essential to perform accurate and reliable tests to ensure proper laboratory diagnosis. The objective of safety awareness and practices in laboratories assure laboratory managers, scientists and support staff that through adopting proper engineering and administrative controls, policies and practices and use of personal protective equipment, they can handle most biohazardous materials without undue risk to themselves, their colleagues or the environment. Laboratories that are well organized and procedurally disciplined are not only safe but are also scientifically efficient.

Sample management is an integral part of a Laboratory Quality Management System (LQMS). The quality of laboratory tests depends on the quality of samples used for testing; therefore, laboratories need to be proactive in ensuring that samples received for different laboratory procedures meet all the standards required to produce accurate

test results. In addition, the pre- and post- sample storage and inventory is a crucial component of the laboratory inventory management system.

Laboratory results directly influence therapeutic decisions and can have significant impact on patient care and outcomes as well as compliment the epidemiological investigations for public health interventions. Therefore, accurate and timely laboratory results must be provided to ensure effective treatment and public health actions. Inaccuracies in laboratory results may prolong hospital stays and increase laboratory and overall healthcare costs. Inaccuracies can also affect laboratory efficiency, leading to repeat testing causing a burden on personnel, supplies, reagents and also waste production.

COMPONENTS OF A SAMPLE MANAGEMENT SYSTEM

Written policies for sample management must be established and reflected in the laboratory SOPs. Components to be addressed may include:

a. Information needed on requisitions or forms;
b. Handling urgent requests;
c. Details of sample collection procedure and time, labeling, preservation and transport;
d. Safety practices (leaking or broken containers, contaminated forms, other biohazards);
e. Evaluating, processing, and tracking samples;
f. Storage, retention, and disposal.

All personnel should undergo training and records should be kept.

IMPLEMENTATION OF A LABORATORY INVENTORY MANAGEMENT SYSTEM

The inventory management system can be implemented in three phases:

1. Pre-test or pre-analytical archiving.
2. Post-test or post-analytical archiving and security of biohazard materials.
3. Sample/specimen disposal.

Pre-test Archiving

Laboratories should prepare a handbook to ensure that all samples are managed properly and that persons collecting or receiving samples have needed information. This handbook should describe the complete process including all the procedures and precautions involved in a specific sampling scheme. It should be made available at all sample collection and receiving areas, including those away from the laboratory. All laboratory staff should also be well acquainted with the information in the handbook. The handbook is an important laboratory document, which needs to be kept up-to-date and referenced in the laboratory's quality manual.

Sample Labeling

Each sample collected or received at the laboratory should be clearly labeled with identification along with a standard questionnaire – a laboratory request form or “Laboratory Investigation Form”. The minimum details to be included in the form should include:

1. Patient's name;
2. Age and gender;
3. Address and contact number of the patient;
4. Name of the hospital referring sample for laboratory investigation (may include ward or unit);
5. Clinical presentation;
6. Test requested;
7. Time and date of sample collection;
8. Name and initials of the person collecting the sample;
9. A unique identification number – this might be a hospital number, or a number assigned by the laboratory.

Verification of quality

Before the sample is processed in the laboratory, there are several steps required prior to testing. These pre-examination/ pre-analytical steps include: documentation of the sample (type of sample, origin of sample, reason for testing, condition of the sample), proper labelling of the sample, and entering into a database for tracking.

The test request form must be complete and include all necessary information; recording sample information into a register or log; enforcing policies and procedures for handling sub-optimum samples, including sample rejection, when necessary.

In case a sample needs to be rejected, a process should be in place to ensure that all the information is documented. This may include: Who certifies the rejection (Director?), Why? What happens next? Immediate communication with the submitter? via phone, email, etc.

Register or log

The laboratory should keep a register (log) of all incoming samples. For this purpose, a master register may be kept, or each specialty laboratory may keep its own sample receiving register. Upon receipt, assign the sample a unique laboratory identification number – write/print the exact identical number on sample and the requisition form. If computers are used for reports, enter the information into the computer. The register should include:

1. Date and time of sample collection;
2. Date and time of sample received in laboratory;
3. Sample type;
4. Location where the sample originated
5. Patient name and demographics, as required;
6. Laboratory assigned identification or number;
7. Tests to be performed.

Post-test Archiving and Security of Biohazard materials

The stocks of biological materials must be maintained in locked freezers, refrigerators and/or liquid nitrogen containers as per the sample's viability, stability requirements and purpose of testing. It is necessary to maintain an inventory of all such materials present in the laboratory at any given time. This inventory should display:

1. Current quantity of a particular material available onsite;
2. Date and amount of material removed from storage;
3. Person removing the aliquot from storage;
4. Purpose of use;
5. Quantity remaining.

The laboratory supervisor must develop certain mechanism to ensure that only designated technically skilled personnel are authorized to handle biohazard materials archived in a laboratory.

Sample storage

Each laboratory should develop a policy for retention of necessary biohazard materials. The inventory of stored samples should be reviewed at specified intervals to determine their requisite discard time. The inventory must include the minimum information required against each sample such as:

1. Description of samples to be stored;
2. Retention time;
3. Location - consider ease of access;
4. Conditions for storage, such as atmospheric and temperature requirements;
5. System for storage organization;
6. Accession number;
7. Test results;
8. Reasons for archiving (for example: unique sample, ongoing epi investigation, validation sample);
9. Power back-up.

Some samples may need to be retained for longer periods. The needs for the stored materials must be evaluated periodically and those not required further must not be kept unnecessarily and compromise the storage space.

Frozen sample and thaw cycles must be monitored, as samples may deteriorate with these conditions. An organized, accessible system using computer tracking would be useful to maintain the inventory of the archived samples.

Sample disposal

The laboratory is responsible for ensuring safe disposal of all laboratory waste. To ensure proper disposal of patient samples:

- develop a policy for sample disposal; apply local, as well as country regulations for disposal of medical waste; and
- establish and follow procedures to disinfect samples prior to appropriate disposal.

SAMPLE REFERRAL TO ALLIED LABORATORIES AND COLLABORATORS

When referring samples to other laboratories for testing, it is important to obtain information about the detailed procedures from each laboratory where the sample is being referred. The responsible staff should ensure that the sample is labelled correctly, stored in the correct container and is accompanied by a requisition form that specifies the

required test(s), and includes the sending laboratory's contact information. The staff should carefully monitor samples that are referred while documenting and keeping a record of all tests / samples referred, date of referral, name of person and information about the requisite test(s). Results received for each referred sample also must be documented and reported with their TAT and any problems encountered.

MAIN CONSIDERATIONS FOR LABORATORY INVENTORY MANAGEMENT SYSTEM

1. All potentially hazardous biological materials must be inventoried prior to long-term storage in any freezer, refrigerator, cold room, or other location. This requirement applies to all kinds of biological materials of any origin, e.g. human, animal or environment. A spreadsheet template necessary for recording inventory data must be designed, reviewed and approved by the laboratory supervisor.
2. The inventory process is an integral part of the laboratory's biorisk management system. Such inventories must be maintained and updated regularly (typically annually or biannually) using a computerized record.
3. Training of laboratory personnel is an important component in the safe conduct of work with biological agents and recombinant nucleic acid materials. Mandatory training should be ensured by the laboratory manager/pathologist to help the staff attain basic laboratory safety orientation and training requirements. In addition, refresher training conducted annually will ensure that workers remain up to date on all the protocols.
4. Laboratories in which work is performed at BSL-2 and higher must be posted with proper signage. The sign must indicate the assigned biosafety level, biological material(s) in use, special procedures or precautions for entry, PPE, immunizations required (if any), name of the laboratory director, work and emergency contact information.
5. Prior to allowing any support personnel, such as maintenance employees, entering the laboratory, all potentially infectious materials should be appropriately stored, and surfaces should be disinfected. One or more laboratory individuals should be assigned the task to ensure timely completion prior to entrance of support personnel.
6. Annual review and update of potentially hazardous biological material inventories must be certified.

TEMPLATE OF SAMPLE INVENTORY

A template for maintaining a sample inventory is given in Appendix 10. Please note that this template is only for illustration purpose and the template of sample inventory lists may be modified as per the user's needs.

LABELLING OF STORAGE VIALS

The sample vials should be labelled with cryo-pens and arranged in cryo-boxes designed to hold 81 or 100 tubes per box. Vials should be labelled with detailed information regarding sample, sample type, date, etc. Some laboratories find it useful to label all vials with computer printed labels and include a label redundancy such as more

than one way to identify the sample. This is crucial in case that the label is destroyed or rendered unreadable. Newer LIM systems rely on computer barcodes on each vial or on a cryo-box to identify the contents.

LONG-TERM STORAGE OF SAMPLES AT -80°C FREEZER

The information printed on the tags posted on cryo-boxes are matched with the inventory maintained in a computer system or hard copy form to retrieve the information of samples stored in cryo-boxes. The barcodes labelled on each container unit are scanned for detailed inventory of samples stored in each section. This system is utilized for the automatic retrieval of information using a scanner and a computer system.

INVENTORY MANAGEMENT SOFTWARE

Commercial software may be purchased or developed, based on the user requirements, to maintain the inventory of archived samples and implemented in the laboratory for sample traceability and efficient management.

BIBLIOGRAPHY

CLSI/NCCLS. Application of a Quality Management System: A Model for Laboratory Services; Approved Guideline. 3rd ed. GP26-A3. Wayne, PA, NCCLS, 2011. Available at: https://clsi.org/media/1523/qms01a4_sample.pdf.

CLSI/NCCLS. A Quality Management System model for Healthcare; Approved Guideline. 2nd ed. HS1-A2. Wayne, PA, NCCLS, 2004. Available at: http://demo.nextlab.ir/getattachment/a6a37aea-a381-4d32-abe7-a386ba1a933f/CLSI-HS1-A2.aspx.

Guidelines for Healthcare Equipment Donations. Geneva, World Health Organization, 2000. Available at: http://www.who.int/hac/techguidance/pht/en/1_equipment%20donationbuletin82WHO.pdf.

ISO 15189:2007. Medical laboratories—particular requirements for quality and competence. Geneva, International Organization for Standardization, 2007.

ISO/IEC 17025:2005. General requirements for the competence of testing and calibration laboratories. Geneva, International Organization for Standardization, 2005.

Laboratory Quality Management System (LQMS) Training Toolkit, WHO, 2011.

Sample Tracking. Available at: https://www.elabjournal.com/sample-tracking/.

Chapter 17

Shipment/Transport of Specimens

Shamsul Arfin Qasmi, Karachi Institute of Medical Sciences, Pakistan
Julie Pavlin, National Academies of Sciences, Engineering, and Medicine, U.S.

INTRODUCTION

This chapter provides guidance to facilitate the transportation of infectious, diagnostic and exempt substances whether by post, road, sea, rail, or air route. Infectious substances are materials which are known or are reasonably expected to contain pathogens. A pathogen is a microbe including bacteria, rickettsiae, viruses, fungi and parasites, and other pathogenic agents such as proteinaceous infectious particles known as prions, which are known to cause illness in man or animals.

DEFINITIONS

Infectious substances are divided into three categories:

1. Infectious Substances Category A
2. Biological Substances Category B
3. Exempt Substances

CATEGORY A (INFECTIOUS SUBSTANCES)

Category A is defined as a substance which can cause an infectious disease when exposure occurs during transportation. This exposure can cause permanent disability or fatal disease in otherwise healthy humans or animals. The United Nations identification number, "UN 2814" has been assigned to Category A infectious substance which meet the above criteria and can cause disease in humans or both in humans and animals. The United Nations identification number "UN 2900" has been assigned to Category A infectious substance which meet the above criteria but can cause disease in animals only.

CATEGORY B (BIOLOGICAL SUBSTANCES)

Category B is defined as infectious material which does not meet the criteria for inclusion in Category A. These are usually diagnostic specimens such as blood, tissue and excreta, where the patient is not known to have a serious disease that can be readily transmitted. Category B has been allocated UN 3373 "Biological Substance". Other designations such as "Diagnostic specimens" and "Clinical specimens" previously assigned to this category are no longer used to avoid confusion.

EXEMPT SUBSTANCES

A sample which does not contain infectious substances, or the substances are not likely to cause disease in animals or humans. Due to decreased risk, these samples do

not have to follow guidelines for dangerous goods. Exempt substances have the following properties:

1. Do not contain infectious substances, or they are unlikely to cause disease in humans or animals.
2. Specimens that contain microbes that are not able to cause infection in humans or animals.
3. Pathogens which have been deactivated, disabled or neutralized, so that they no longer remain a threat to human and animal health.
4. Samples collected from the environment (including water and food) that are not capable of causing a significant risk of infection in humans and animals.
5. Blood or blood components for the purpose of transfusion.
6. Dried blood spots and fecal occult blood screening samples.
7. Patient specimens with minimal likelihood that pathogens are present – package marked “exempt human specimen” or “exempt animal specimen.”
8. Healthcare or laboratory wastes which have been decontaminated.

TAXONOMY & CHARACTERIZATION

Types of specimens requested for transport or transfer by air, rail, road or ship include the following:

1. Cultures: Cultures of pathogens intentionally propagated. These do not include patient specimens.
2. Patient specimens: Consist of samples collected directly from humans or animals for research purposes, diagnostic evaluation, investigations, treatment and prophylaxis. These samples include secretions, blood, serum, plasma, excreta, cellular parts, tissues and tissue fluid swabs taken from any part of the body.
3. Products of biological nature: These products are derived from living organisms and are used mainly for prevention, treatment, or diagnosis of disease in humans and animals, or for research and development purposes. They also include complete and incomplete products such as vaccines.
4. Genetically modified organisms: Organisms in which chromosomes have been altered through genetic engineering/manipulation. Shipment is the same as with other infectious agents. UN 3245 identification number is assigned to those GMOs who do not fulfill the criteria for infectious substance.

MEDICAL/CLINICAL WASTE

The waste material generated in response to medical treatment or biological research of humans and animals. This waste which contains infectious substances of Category A is assigned UN 2814 and UN 2900 as noted above for human or animal pathogens, respectively. Waste containing Category B substances is assigned UN 3373, and regulated medical waste or not otherwise specified is assigned UN 3291 as per UN identification instructions.

SHIPPING REGULATIONS

The material of triple packaging provides three layers of control and containment to protect the substances being shipped. These layers are primary, secondary, and tertiary containers as shown in Fig. 16-1 (see Appendix 7 for more information).

Category A

Fig. 16-2 provides an example of the triple packaging system recommended and standardized by the UN for samples designated in Category A.

The packet contains:

- A water tight container.
- A water tight secondary receptacle (to contain any spilled liquid materials).
- An absorbent material within the secondary receptacle which is capable of absorbing any leakage of sample in the primary container.
- A rigid outer packaging (capable of protecting the contents).

It is mandatory that the structure of the complete packet is able to withstand the following performance tests:

- Primary container is leak proof;
- Secondary container is also leak proof;
- Outer container is rigid;
- Capacity to bear pressure of 95 kPa;
- Drop test from a height of 9 m;
- Puncture resistant at 7 kg pressure.

In addition to the above requirements, the package must contain the following:

- UN identification code;
- A certified/trained technician must prepare the contents for shipping;
- Proper shipping documents including emergency response information.

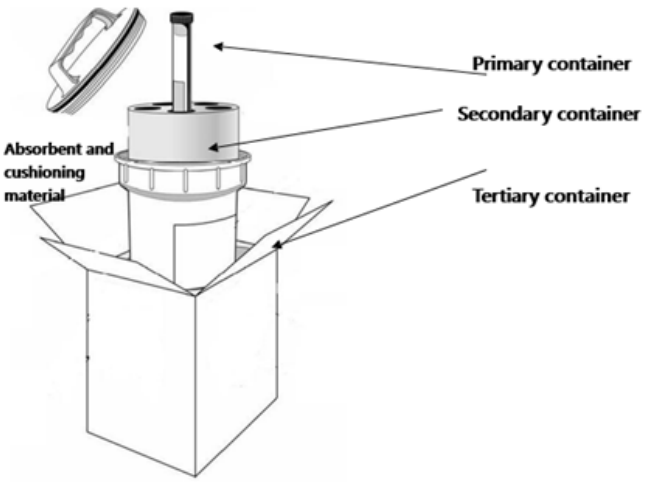


FIGURE 17-1: The basic concept of triple packaging.
(Source: IATA, Montreal, Canada)

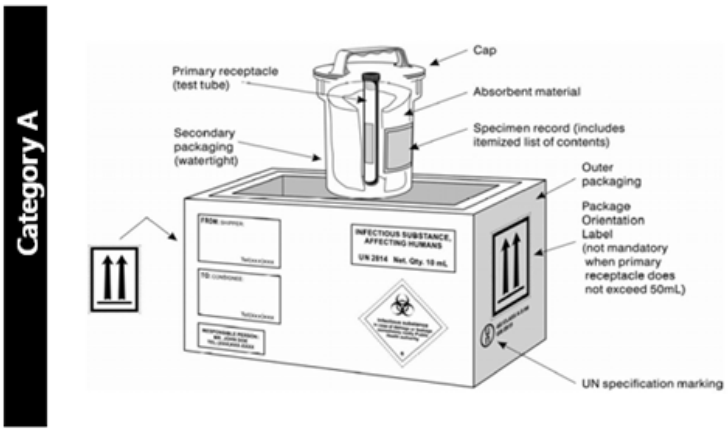


FIGURE 17-2: Example of triple packaging system for the packaging and labelling of Category A infectious substance. (Source: IATA, Montreal, Canada)

Category B

Fig. 17-3 provides an example of the system for packaging of infectious substances for Category B. It is important that this category should fulfill the following criteria before it is packed for delivery or transportation:

- Primary container is leak proof.
- Secondary container is leak proof.
- Pressure tested at 95kPa.
- Either secondary or outer container is rigid.
- If transport is by air, the outside receptacle must be robust.
- Drop tested from 1.2 m.
- The minimum outer-container size dimension equals 100 mm (4 inches).
- Capable of withstanding shocks during transportation.
- Able to absorb vibrations, changes in temperature, and humidity in addition to pressure.
- Secondary package must contain enough absorbent material.
- Accompanied by all the required information consisting of name of the responsible person/institution with address and telephone number.
- A written shipping article.
- Emergency response information.

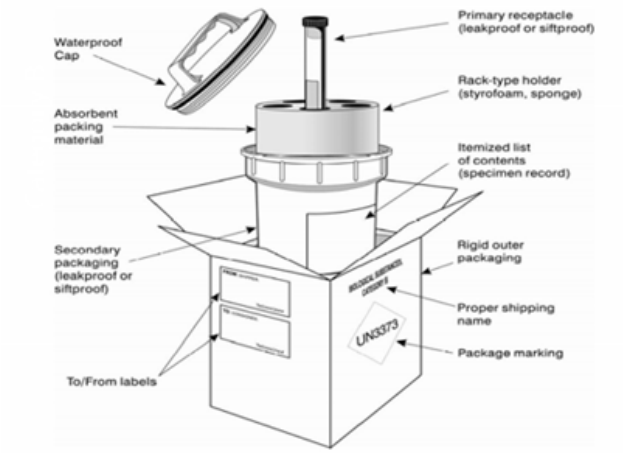


FIGURE 17-3: Standard triple packet system as per WHO classification for packaging and labelling. (Source: IATA, Montreal, Canada)

Exempt Substances

The receptacle for these types of samples is shown in Fig 17-4 and must have the following properties for transport:

- Primary container is leak proof;
- Secondary container is leak proof;
- Outer packing with adequate strength.

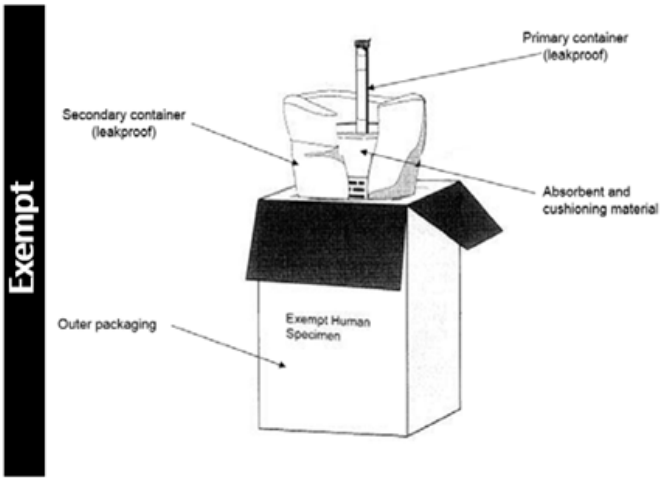


FIGURE 17-4: Illustrates the basic design of packaging system for exempt substances (Source: IATA, Montreal, Canada)

STEPS FOR PACKAGING SAMPLES

TABLE 17-1: Regulations of Transportation

S.No.	Procedure
1	Shape outside receptacle
2	Insert inner lining
3	Remove cap of secondary receptacle
4	Place equivalent material for absorption if spill occurs
5	Don disposable gloves
6	Insert cushion material round the primary tube
7	Place primary container into secondary container
8	Doff disposable gloves
9	Secure and close secondary container
10	Place secondary container into inner lining (and outer container)
11	Insert laboratory test instructions
12	Pack and close the tertiary container
13	Confirm that Category A package labeling, and marking has been done

Regulations for international and domestic transport of infectious substances are intended to prevent the discharge of infectious substances when they are in transit, and to protect the public, laboratory and shipping workers, environment and other property from the harmful effects of these materials if they are exposed due to some error in packaging. Rigorous packaging requirements and hazard communication offer protection during transport. The packaging should be designed so that it is capable of withstanding rough handling, and other stresses which may be experienced during transportation, such as pressure and temperature changes, vibration, and moisture. In an emergency situation, information regarding material transported and proper hazard communication should be available to enable the personnel responsible for transport to promptly and correctly identify the specimen and its nature so that an emergency response can be immediately launched accordingly. Proper training for shippers and carriers on these regulations is beneficial so they can correctly make shipping documents and respond to the dangers and risks in case of exposure. One such course is freely available online from the US Centers for Disease Control and Prevention (https://tceols.cdc.gov/). Certification courses expire after a set time, usually 2 years, and then have to be taken again to maintain qualification.

INTERNATIONAL REGULATIONS

By flight:

Safe Transport of Dangerous Goods by Air Technical Instructions printed by the International Civil Aviation Organization (ICAO) are the international regulations. These are followed by most of the airlines worldwide.

The International Air Transport Association (IATA) and Dangerous Goods Regulations (DGR) incorporate the ICAO provisions. These rules are for all flights intended for international routes. In reference to national routes, the local Civil Aviation Authorities CAAs formulate and apply national guidelines.

By Railway:

International Carriage of Dangerous Goods by Rail (RID) regulations are for European countries, the Middle East and some countries in North Africa. Pakistan is currently developing these guidelines.

By Motor Vehicle:

For motor vehicles, the International Carriage of Dangerous Goods by Road is a European agreement and is enforced in 40 countries.

By Vessel transport:

The International Maritime Dangerous Goods Code published and issued by the International Maritime Organization (IMO) is compulsory in 155 contracting parties to the International Convention for the Safety of Life at Sea (SOLAS).

By Postal service:

The letter post manual published by the Universal Postal Union (UPU) echoes the United Nations recommendations using the ICAO provisions as the basis for shipments. The WHO works in an advisory capacity to the United Nations Committee of Experts on the Transport of Dangerous Goods (UNCETDG) and ICAO.

NATIONAL REGULATIONS

Pakistan has adopted the United Nations Model Regulations as national dangerous goods legislation.

SHIPPING IN PAKISTAN

Regarding international obligations and implementation of national regulations in Pakistan, local courier services have started following these regulations.

In Pakistan, courier agencies are following rules and regulations in strict compliance with international requisites for both categories “A” & “B”. Employees of these courier services and companies who are involved in transfer and transport of these substances must receive proper training along with the technical staff working in healthcare facilities to avoid any inadvertent exposure of infectious substances.

All steps in shipping of such substances must be documented, and the package tracked via written records from the time it is shipped. The ownership remains with the generator of the shipment.

Training in shipment of infectious agents is mandatory for shipment of Category A substances and this training should be provided on an institutional basis. The National Institute of Health (NIH) and the Pakistan Biological Safety Association (PBSA) are playing pivotal role in organizing these trainings to the target audience comprised of

laboratory managers, pathologists, microbiologists, technologists, technicians and phlebotomists.



FIGURE: 17-4: Sample Box of infectious substances in Category A
Source: IATA Guidelines 2011

BIBLIOGRAPHY

Biosafety in Microbiological & Biomedical Laboratories. 2009. 5th Ed. Department of Health and Human Services, Centers for Disease Control & Prevention and National Institutes of Health, US.

Division 6.2 Infectious Substance Shipping Guide: Classification, Packing, Marking and Labeling. Massachusetts Department of Public Health. William, A.H. State Laboratory Institute 2012.

ECOSOC Sub-Committee of Experts on the Transport of Dangerous Goods (TDG). UNECE. Available at: http://www.unece.org/trans/main/dgdb/dgsubc/c3age.html.

Guidelines for the Safe Transport of Infectious Substances and Diagnostic Specimens. WHO Division of Emerging and Other Communicable Diseases Surveillance and Control 1997.

Infectious Substances Shipping Guidelines 58th Ed. IATA Dangerous Goods Regulations 2017.

Laboratory Biosafety Manual. 2004. 3rd Ed. WHO

The Dangerous Goods Regulations of the ICAO Technical Instructions for the Safe Transport of Dangerous Goods by Air. ICAO Ed.: 2105-2016.

Transporting Infectious Substances Safely. Federal Register. Hazardous Materials: Infectious substances; Harmonization with the UN recommendations. US Department of Transportation 2006.

USPS Packaging Instruction 6C, Category B Infectious Substances.

WHO Guidance on Regulations for the Transport of Infectious Substances. Communicable Disease Surveillance and Response. September 2005.

Chapter 18

Equipment Performance in Relation to Quality Assurance

Ashok Kumar Tanwani, Pakistan Institute of Medical Sciences; Muhammad Yousaf Janjua, Pakistan Institute of Medical Sciences, Islamabad; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

SCOPE

All laboratories should use good clinical practices as they are performing tests on various biological samples for diagnosis, disease control, patient care and research. The tests belong to various sections:

- Hematology & Blood Banking
- Clinical Pathology
- Microbiology & Serology
- Clinical Biochemistry
- Molecular Pathology and Molecular Biology
- Histopathology and Cytology
- Immunology (Immunohematology and Immuno-biochemistry)

SELECTION OF EQUIPMENT

Selection of right equipment for lab is the key step in management of equipment. Criteria for selecting laboratory equipment include:

- What is the purpose of using equipment and how it will be used?
- Does the current or potential future case load justify the purchase of specific equipment?
- What are the performance features of equipment?
- Is the accuracy and reproducibility sufficient for testing?
- What are the space and electrical requirements?
- Is the cost of the equipment within the budget limits of lab?
- Are reagents readily accessible or difficult to procure?
- Can laboratory staff be trained in the operation of the instrument?
- Are instructions for user clear?
- Does the distributor earn a good reputation?
- Does the equipment carry a manufacturer warranty?
- Are after sales services reliable?
- Is a service workshop available locally or nationally?
- Are there occupational or environmental safety issues that need to be addressed prior to utilizing the equipment?

INSTALLATION OF EQUIPMENT

Verification of physical necessities checklist e.g. power, area, ventilation and water supply requirements must be fulfilled before installation of equipment according to specification of the equipment provided by manufacturer. Other things to be considered are:

- Prior to beginning of the installation process, responsibilities of vendor for installation should be verified in writing;
- A checklist of performance specifications to be expected should be prepared for quick verification after installation of equipment;

If equipment is installed by the laboratory;

- It should be checked that all parts are present in package contents;
- Copy of software should be made which is part of system;
- Equipment should be used after complete installation, performance should be verified, and testing personnel must be trained;

GETTING THE EQUIPMENT READY FOR SERVICE

After Installing the Equipment

The following points are addressed after installation but before starting the equipment for service:

- Assign maintenance and operational responsibility;
- System should be developed to keep record about use of parts and supplies;
- A written plan should be implemented for calibration, performance verification, and correct operation of the equipment;
- Establishment of scheduled maintenance programme e.g. daily, weekly and monthly or yearly should be kept as record;
- Operational training should be given to all operators and only trained operators should be authorized to operate the equipment;
- All operators should be trained for maintenance program including calibration, verification and operating procedures as inventory record;

Equipment Calibration

Manufacturer's directions should be followed properly while performing the calibration of the instrument. When instrument is initially put into service, calibration stability of different parameters should be determined based on the manufacturer's instructions.

Performance Evaluation

Accuracy and precision of instrument should be evaluated prior to testing of patient specimens. In addition, evaluation of test procedures using kits or lab instruments is required for the capability of disease detection (sensitivity, specificity, positive and negative predictive value) and to set normal and reportable ranges.

Validation of new equipment, reagents and associated techniques

Verification of manufacturer's claims written in inserts or manuals about performance should be carried out. It should be ensured whether the same results are being obtained using the kits or equipment in the laboratory.

To verify performance following steps should be followed:

- Samples should be tested with known values and results should be compared to the reference value;
- Temperature must be stable and uniform if instrument is temperature controlled;

Validation process is important if equipment and associated techniques are new. In order to determine that expected results are obtained or not, samples are run in parallel for validation purpose by using old and new analyzers and procedures for a period of time. Complete record of the procedures used for validation should be kept.

IMPLEMENTATION OF EQUIPMENT MAINTENANCE PROGRAMME

Preventive Maintenance

Preventive maintenance covers systematic and routine cleaning, adjustment and replacement of parts of equipment according to the schedule. Manufacturer generally recommends a set of equipment maintenance tasks which should be performed at regular intervals i.e., daily, weekly, monthly or yearly. If these recommendations are properly followed, equipment will perform at maximum efficiency and augmented life span. This is helpful in avoiding:

- Wrong results;
- Delayed reporting;
- Reduction in output;
- Heavy expenditures on repairs.

According to the SOPs, a label is pasted on instrument which reminds about the next maintenance or service.

Equipment Inventory

Inventory log of all the available equipment is maintained in the laboratory and updated with details of new equipment. Inventory log of all equipment should exhibit the following record:

- Type make and model number of equipment;
- Purchasing date of equipment and status (new, used or reconditioned);
- Contact information of vendor;
- Availability of documentation, spare part and maintenance contract;
- Warranty period;
- Inventory number indicating the year of acquisition e.g. use the style “YY-number” (04-001, 04-002, etc.).

Spare parts Inventory

Spare parts inventory should include the following information:

- Name and number of different parts;
- Average usage and minimum availability requirement in stock;
- Price of the part;
- In and out stock log;
- Balance quantity of each part in the inventory;

QUALITY CONTROL

Quality control (QC) is a statistical procedure which monitors and evaluates laboratory processes for accurate results. QC reagents should be used to check whether an instrument is operating within the defined limits. QC reagents contain different levels of controls (in the normal, low, and high range) and should be assayed daily in clinical chemistry and haematology labs.

Performance of test system is done by running daily quality controls and comparing their results with the defined range of quality control values. Mean and standard deviations are calculated from testing of control products on regular basis both for normal and abnormal ranges. Mean is calculated by adding all values for that specific control divided by their total number of values:

$$\text{mean} = \frac{\sum x_i}{n} = \bar{x}$$

Standard deviation or precision is used to quantify that how close the controls values are and is calculated by the formula:

$$s = \sqrt{\frac{\sum (x_i - \bar{x})^2}{(n - 1)}}$$

Large or unexpected changes in the mean standard deviation can lead to imprecision and may be due to the analytical process malfunctioning due to any of the following reasons:

- Change in reagent lot or composition of reagent;
- Instrument malfunction / Routine or scheduled maintenance not performed;
- Change of technician;
- Pipetting errors;

Documentation of quality controls require a QC chart where mean and SD of each level of control is plotted along with the following:

- Month and date wise;
- Name of test;
- Units;

- Operator name;
- Instrument nomenclature;
- Reagent lot;

Having a detail log of QC measurements will ensure that the machine has been running correctly over time and will help identify errors. A **random error** is statistical fluctuation (in either direction) in the measured data due to the precision limitations of the measurement device. Random errors usually result from the experimenter's inability to take the same measurement in exactly the same way to get exact the same number. A **systematic error**, by contrast, is reproducible inaccuracy that is consistently in the same direction. Systematic errors are often due to a problem which persists throughout the entire experiment. This will result in the mean values tending to gradually change (increase or decrease) and may indicate an issue with the machine or QC reagents. The machine manual must be consulted to determine the cause of the error. When machines need maintenance or routine cleaning, a back-up plan should be in place for processing samples those are received in the laboratory.

BIBLIOGRAPHY

Cembrowski, G.S., Carey, R.N. Laboratory Quality Management: QC & QA, ASCP Press (1989).

Cooper, G., and Gillions, T. Producing Reliable Test Results in the Medical Laboratory (2007).

Davies, O.L., and Goldsmith, P.L. Statistical Methods in Research and Production, New York (1984).

Howanitz, P.J., and Joan H. Laboratory Quality Assurance, McGraw-Hill Book Company (1987).

Kaplan L.A., Pesce A.J. Theory, Analysis, Correlation Clinical Chemistry. 5th ed. pp 470-473.

National Committee for Clinical Laboratory Standards. Internal Quality Control: Principles and Definitions; C-24A.

Westgard, J.O., Barry, P.L., Hunt M.R., Groth, T.A. Multi-Rule Shewhart Chart for Quality Control in Clinical Chemistry; Clin. Chem. 1981;27(3): 493-501.

Westgard, J.O., Koch, D.D., Oryall, J.J., Quam, E.F., Feldbruegge, D.H., Dowd, D.E., Barry, P.L. Selection of Medically useful Quality Control Procedures for individual tests done in a Multi-Test System; Clin. Chem. 1990;36:230.

Westgard, J.O., et al. Combined Shewhart – CUSUM Control Chart for Improved Quality Control in Clinical Chemistry; Clin. Chem. 1977;23(10): 1881-1887.

Weisbrot, M.D. Statistics for The Clinical Laboratory; J.B. Lippincott Company, Philadelphia (1985).

CHAPTER 19

Troubleshooting, Service, Repairing and Retiring the Equipment

Ashok Kumar Tanwani, Pakistan Institute of Medical Sciences; Muhammad Yousaf Janjua, Pakistan Institute of Medical Sciences, Islamabad; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

SOURCE OF THE PROBLEM

Equipment can develop different issues ranging from very minor to major e.g. QC or calibrator value drift or obvious flaws in the functionality. Advance training of the operators to troubleshoot equipment problems in order to make it functional immediately and resume testing is a mandatory requirement.

TROUBLESHOOTING

A flowchart is provided by manufacturer that can be helpful in identifying the sources of problems. Consider the following questions:

- Is the problem concerned with poor sample? Sample collection and storage was proper or not? Are factors like turbidity or coagulation affecting the performance of instrument?
- Have the reagents any problem? Is storage proper and are within expiry date? Has a new lot of reagents been introduced without re-calibration of instrument?
- Are electrical supplies or water problematic?
- Is the equipment problematic?

Operators should follow the troubleshooting flow chart provided by the manufacturer or contact the manufacturer technical service department. Manufacturer's instructions should be reviewed to verify that all procedures are being followed correctly.

WHEN PROBLEMS ARE NOT RESOLVED

If the technical staff is unable to identify the problem, alternate may be used for continuation of lab tests until the repair of the original:

- Backup instruments;
- Manufacturer should be asked to provide a replacement instrument during repair period.

Faulty equipment should never be used. Contact manufacturer or technical expert for immediate action and place a tag of being non-functional over the equipment.

SERVICE AND REPAIR

Supplier is responsible for performing service and repair of equipment periodically. Remember that some warranties are conditional, and in that case, repairs are handled only by the manufacturer. In-house biomedical service engineers are available in large facilities for performing maintenance and repair of equipment. The vendor should take the responsibility for acquaintance of the lab engineers with the newly inducted equipment.

RETIRING AND DISPOSING THE EQUIPMENT

A clear policy and protocol should be available for retiring of the old laboratory equipment. Retiring is done when it is confirmed that the equipment is beyond repair, parts are not available, cost of repair more than the new equipment, or when it is outdated. Retired equipment should be disposed of according to the protocol considering any potential biohazards and following all safety disposal procedures. It should also be endorsed in the inventory.

DOCUMENTATION OF EQUIPMENT MAINTENANCE

Defining Documents and Policies for Record keeping

Maintenance procedures and policies should be defined in appropriate documents for allowing thorough evaluation of any problems that may arise. Equipment maintenance documents are available with all major equipment. Maintenance of commonly used smaller equipment may be managed by using equipment maintenance document that generally deals with all such equipment available in the lab. Following is included in equipment maintenance document:

- Instructions given in steps for routine maintenance;
- Instructions for carrying out function checks, performance frequency, and recording the results;
- Direction for calibration of the instruments;
- Guide for troubleshooting;
- Service and repair which is done by manufacturer;
- List of any special items required for use and maintenance e.g. spare parts.

Recording Maintenance Information

A dedicated logbook should be kept in the lab for all equipment in which characteristics and various maintenance elements are documented, like:

- Schedule and activities of preventive maintenance;
- Function checks and records of calibration;
- Any maintenance done by the manufacturer;

The following should be recorded about the problem:

- Problem occurring and removal for service dates;
- Cause of failure or breakdown;
- Corrective action by the manufacturer;
- Equipment taken and return from workshop date.
- Problem resulted in any change for procedure of maintenance or function checks.

Availability of logbook of any equipment should be there for review during its entire life (See Appendix 8).

BIBLIOGRAPHY

DAIDS Guidelines Good Clinical Laboratory Practice Standards. Available at: https://www.niaid.nih.gov/sites/default/files/gclp.pdf.

Laboratory Quality Management System. Version I.I Geneva, World Health Organization 2011: 36-48.

SECTION IV:
QUALITY MANAGEMENT SYSTEM

Chapter 20

Standards in Clinical Laboratories

Ayesha Junaid, Shifa College of Medicine; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

"Standards are critical. The more standardization we can bring to the laboratory, the more consistent results are." Greg Miller, PhD

STANDARDS

Specific requirements to maintain the quality and competence in the clinical laboratories make up the "standards". These "standards" are the measurements by which the accrediting and regulatory bodies determine that a clinical laboratory meets a defined level of operation. These standards are periodically reviewed and re-defined to meet the current and emerging clinical needs. Patients on the other hand, also have certain standards or criteria in mind which may not necessarily be technical.

In Pakistan, Pakistan National Accreditation Council (PNAC) working under the Ministry of Science & Technology, currently applies ISO 15189-2012 standards for accrediting medical laboratories. This standard is currently being used for accrediting clinical laboratories in approximately 60 other countries all over the world.

Other contributing sources for the current clinical laboratory standards are

- College of American Pathologists (CAP). www.cap.org
- International Organization for Standardization (ISO) 9000. www.iso.org
- ILAC Guidance documents (G Series) www.ilac.org/publications-and-resources
- The Clinical & Laboratory Standards Institute (CLSI). www.clsi.org

LABORATORY STANDARDS

Laboratory standards generally consists of two major components

- Management Standards
- Technical Standards

Management Standards

Organizational Standards

Organizational standards are those processes and procedures defined by the organization that ensure a clear management scheme and efficient laboratory operations at all times. These allow for the smooth functioning of the laboratory and that all personnel understand their roles and to whom they are supposed to report issues, concerns, or problems. This management ensures smooth internal and external communication.

A laboratory organization chart is helpful to communicate with the management in a lab. This helps to ensure that service remains uninterrupted in the event of an emergency. For the key management post, an alternate expert should be clearly indicated in case of absence of the primary person. In addition, alternate arrangement of supervisory responsibilities should be clearly marked. It is important to remember that the person temporarily in charge (interim) should have both the training and the authority to act effectively in the temporary management role.

Laboratory management should periodically perform a "need analysis" after reviewing employee and customer feedback and suggestions. Clinical laboratories must consider clinicians, patients and community health department as customers and regular input (suggestion box/feedback box) should be taken to improve service standards.

Personnel Standards

These standards define qualities which the clinical laboratory workers must exhibit during the pursuit of their professional duties. Laboratory performance and reputation are built on personnel performance. The professionalism of the technical team, including, time, discipline, command on skill and communication ability can enhance the quality of practices behind the scene. This is true for all team members; from the front desk workers to the bench technicians.

All laboratory team members should be hired through a transparent process with clear credential and experience-based criteria. Position descriptions should clearly list the necessary qualifications and experience for both initial and subsequent roles in the laboratory. The number, level of competency and training for all the staff in a clinical laboratory should meet the required level of working. Periodic assessment of the employees is necessary to assure that competency of laboratory personnel is maintained over time. From technical bench to management level, continuing training and upgrading of the knowledge and communication skill is mandatory.

Advisory Services Standards

These standards laydown the basis of identifying and rectifying any weakness/error in the present working environment. Assigned management team/section should continuously review and produce improvement for standard service delivery. System should be in place for identifying non-conformities and error reporting. Preventive and corrective actions to be taken should be identified and implemented in time in case of any incident reports. Continuous process improvement should be built into laboratory operations. Patient guidance with regards to different services should be available in print and/or in electronic form. Printed information about any diagnostic procedure (bone marrow biopsy/FNAC) may also be available in local languages (Urdu, Sindhi, Pushto, Balochi, etc.)

TECHNICAL STANDARDS

Physical Standards

These standards define template to buildup clinical laboratories in order to ensure efficient workflow and workers' safety and comfort. It is important that different departments of the clinical laboratory are designed for safe and efficient workflow. Proper

ventilation, light and temperature control of the facility must be ensured. Back ground areas such as storage spaces for post-analytic specimens, controls and reagents, changing rooms, cleaning equipment placement area) should be clearly defined and separate from the working benches.

Excellent liaison among supporting departments of clinical laboratory (purchase and procurement, inventory, LIS, and marketing departments) should be ensured in order to provide seamless and smooth clinical service. Vendor orders should be placed on an annual basis to minimize cross borders processes/delays of the control materials and reagents in all possible situations. A list of critical items with alternatives should be strictly maintained, in case of delay in the routine procurement channel.

In case of any legal issue with regard to test samples or results, archiving and storage of the relevant material or retrievable electronic record should be maintained (as per laboratory specimen and record storage policy). Backup instruments and contingency plans should be in place and all staff members must participate in regular drills regarding instrument malfunction situations. All laboratory waste should be disposed of according to institutional environment safety protocols.

LIS Standards

These standards can be reviewed in two parts:

1. Software standards essential for appropriate working in clinical laboratories:

The software standards are critical, for a vital and prompt diagnostic service. The laboratory must maintain all test records through LIS including machine and interfaced results, control and calibration files. Electronic records of the panic values and critical results must be available in a retrievable manner. For all clinical tests, age specific reference ranges and relevant comments must be provided next to actual test results. Advanced laboratories can provide computer time-stamped reports along with employee ID verifying the results. If auto-verification is used, then the audit trail must reflect that the result has been verified automatically at a given time and date without manual interference and scrutiny.

Current use of LIS must match policy and procedure documents. The laboratory must have a documented backup system and accompanying procedure for the LIS, in an effort to maintain integrity of data and reduce impact and severity of unscheduled downtimes and damaging events. LIS must have fool proof systems for data protection and recovery in case of hardware and/or software failure for the timely restoration of services. This must include dealing under disaster situations like flood and fire. To all practical extent, LIS should be run in a closed environment to protect participant confidentiality.

Any changes or modifications to the computer system must also be documented, and the laboratory director or designee must approve all changes before they are released for use. In addition, the security of the system must be robust enough to prevent unauthorized personnel from using, copying any data or installing any software. Unauthorized installation of software may expose the system to a security breach, virus, worm, or spyware. It is important that laboratory personnel understand their role in protecting vital laboratory equipment.

2. LIS Standards for the Staff:

When working in a laboratory on a computer system, all users should have a unique User ID. The laboratory must ensure that LIS access is limited only to authorized individuals. Such a User ID should only be assigned to an individual after all suitable training for the computer system and LIS system are complete. User ID must NOT be shared with co-workers. Passwords should be kept confidential and not written down where others may gain access. User ID should be inactivated upon termination of service of an employee. The User ID code once inactivated, should not be used for another employee.

Documentation Standards

These standards highlight which documents a clinical laboratory must prepare and keep the records tidy and meticulous in order to have smooth timely reporting and reconfirmation of reported results.

Following documents are to be made available as a mark of quality organizational structure and personnel:

- Policies (organizational, departmental and personnel);
- Protocols for laboratory tests and analyses;
- Personnel data:
    - Personnel training;
    - License;
    - Competency assessment;
    - Organizational charts (defining reporting channels).

Due to the sensitive nature of some of the documents, system controls and access controls may be necessary. System Controlled Documents and Controlled Access Documents should be clearly defined and available to management and authorized staff only. Uncontrolled documents should not be used for guiding laboratory procedures.

For audit purposes, all records including every test result, instrument log, quality log and data sheets should be kept in a retrievable and safe format in accordance with institutional record keeping policy. In addition, the laboratory must keep document outlining the technical support staff and/or vendor for the system failure including emergency contact information.

Equipment Standards

These standards define the minimum essentials for procuring and keeping laboratory equipment and are directly related to laboratory productivity and valid reporting. All laboratory equipment must be listed in an inventory (purchased /reagent rental). Maintenance log of routine/emergency service should be meticulously kept, including all corrective services performed, and should be available for manager/quality officer review. Backup instruments for all critical laboratory tests should be available in functional condition. Dual electrical supply with "minimum delay time" preferably automatically switching to the backup system should be ensured.

Quality Management System (QMS) Standards

These standards define principles to ensure that quality procedures and processes are adopted by the clinical laboratory in all aspects of service. There should be a fully functional quality department with a designated **Quality Manager/Officer**. There should be a quality policy, with clear objectives and Goals.

The laboratory management shall review and document the existing QMS for adequacy, effectiveness, suitability. The QMS used by a clinical laboratory should be internationally approved or at least recognized at national level. Thus a universal standard of patient service is ensured. For guaranteeing correct and quality results, the laboratory should verify that the principles of best laboratory practice are strictly being followed in pre-analytic, analytic and post analytic phases of testing /reporting. Management review report should be shared with the laboratory staff annually/or more frequently for those in the development phase.

BIBLIOGRAPHY

Clinical & Laboratory Standards Institute (2009). Training and Competence Assessment; Approved Guideline 3rd Ed. [CLSI document GP21-A3, 29(5)].

College of American Pathologists Commission on Laboratory Accreditation, Laboratory General Checklist, 2012.

Good Clinical Laboratory Practice Standards. Ver 3.0; 2013.

Standards for Equipment. Accreditation Checklists 2012. College of American Pathologists Commission on Laboratory Accreditation.

Standards for Personnel & Organization. 42 CFR § 493.1413; and 42 CFR § 493.1451.

Chapter 21

Quality Control in Microbiology Lab

Irfan Ali Mirza, Combined Military Hospital Lahore Medical College

INTRODUCTION

According to ISO, quality is rightly described as the characteristics of a product or service that makes it suitable for the purpose for which it is planned (fitness of purpose). In terms of medical laboratories, Quality Control (QC) can be defined as the constellation of mechanisms used to determine accuracy, reliability and consistency of data, assays or tests performed in the lab. In microbiology lab this is accomplished by assessing the quality of the specimens; monitoring performance of test procedures, reagents, media, instruments and personnel; reviewing test results; and documenting the validity of test methods.

QUALITY CONTROL PARAMETERS

Quality must be measured if it has to be managed. Quality indicators or QC parameters help the health laboratory to define and measure progress. The measurement of quality indicators leads to early detection of system failure which includes all aspects of service – pre-analytic, analytic and post-analytic – so that remedial actions can be taken promptly.

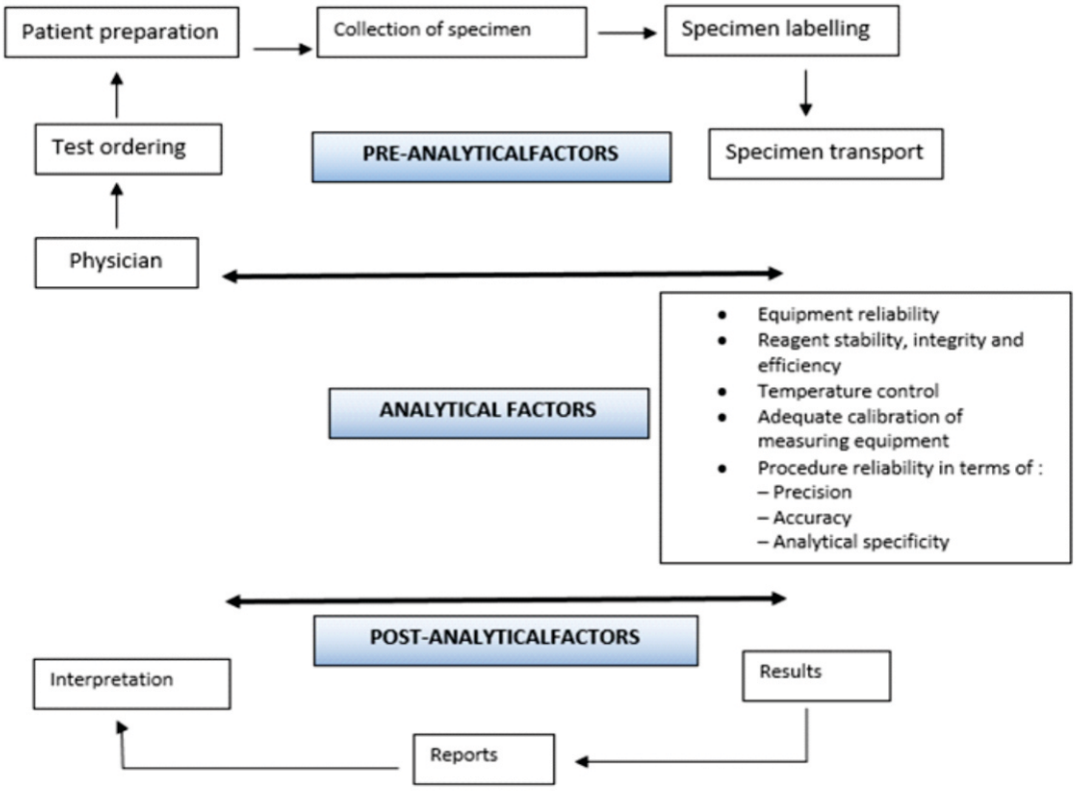


FIGURE 21-1. Quality Control Parameters

QC PROGRAM IN MICROBIOLOGY LAB

QC programs ensure that the information generated by the laboratory is accurate, reliable and reproducible. This can be accomplished by monitoring the following in a microbiology lab:

TABLE 21-1.Quality Control Program Parameters and Guidelines

QC Parameter	Guidelines
Specimen collection and transportation	Provide instructions for collection and transport Label specimen properly Establish criteria for acceptable specimens Establish rejection criteria for unacceptable specimens
Procedural manual	Establish SOPs to define test performance, tolerance limits, specimen acceptability, reagent preparation, QA calculations and reporting Review annually Ensure availability in work area
Personnel	Use sufficient qualified personnel depending upon volume and complexities of work Provide continuous technical education Provide written performance standards Evaluate annually

QC Parameter	Guidelines
QC records	Record all QC results on prescribed forms Report all out-of-control observations to supervisor Note corrective actions on QC form Review QC records monthly
Patient reports	Report only to authorized personnel Notify test requester of important values immediately Provide normal ranges where appropriate Correct errors in patient's reports in timely fashion Retain records for at least two years or as per local requirements
Referral specimens	Use only authorized referral laboratory Include name of reference laboratory on patient's reports
Proficiency testing programs	Participate in appropriate external quality assessment schemes Adopt internal quality assessment programmes
Equipment performance	Document function checks of the equipment Perform as frequently as recommended by manufacturer Document routine preventive maintenance Retain maintenance records for life of equipment
Commercially prepared media	Inspect each shipment for cracked media or petri dishes, haemolysis, unequal filling, excessive bubbles and contamination Document deficiencies, take corrective action, inform manufacturer Perform in-house QC testing
User prepared media	Record amount prepared, source, lot numbers, sterilization method, preparation date, pH, expiration date Check medium for color, consistency, depth or slant, smoothness, haemolysis, contamination, bubbles Test media with QC microorganisms of known characters
Stains, reagents and sera	Label containers as to contents, concentration, storage requirements, date prepared, received/ placed in service, and shelf life Store as per recommendations Test with positive and negative controls prior to use (with each batch, lot number and shipment) Discard appropriately outdated materials and reagents that fail to perform
Commercial kits	Test each new batch, lot and/or shipment Follow manufacturers' recommendations for QC testing
Antimicrobial susceptibility testing	The basic QC procedure involves testing reference strains that have defined characteristics of susceptibility to antimicrobial agents tested Test organisms in pure cultures only Check each new lot of discs for activity before use For disc or dilution tests, test control organisms with each new lot or batch of antimicrobial agents or media and each day the test is performed Control organisms can be tested weekly providing a laboratory can document satisfactory performance with daily control tests Provide written criteria for interpretation of end points or zone sizes Clinical & Laboratory Standards Institute (*CLSI*)

ASSESSMENT OF QUALITY

The retrospective and periodic assessment of quality can be undertaken by an independent external agency or internally by designated staff on behalf of the laboratory management.

TABLE 21-2. Quality Assessment

Feature	Internal Quality Assessment	External Quality Assessment
Nature	Concurrent and continuous	Retrospective and periodic
Performed by	Laboratory staff	Independent agency (e.g. NEQAS, NEQAPP)
Objective	To provide reliable results on day to day basis	To ensure inter-laboratory comparability and improve performance

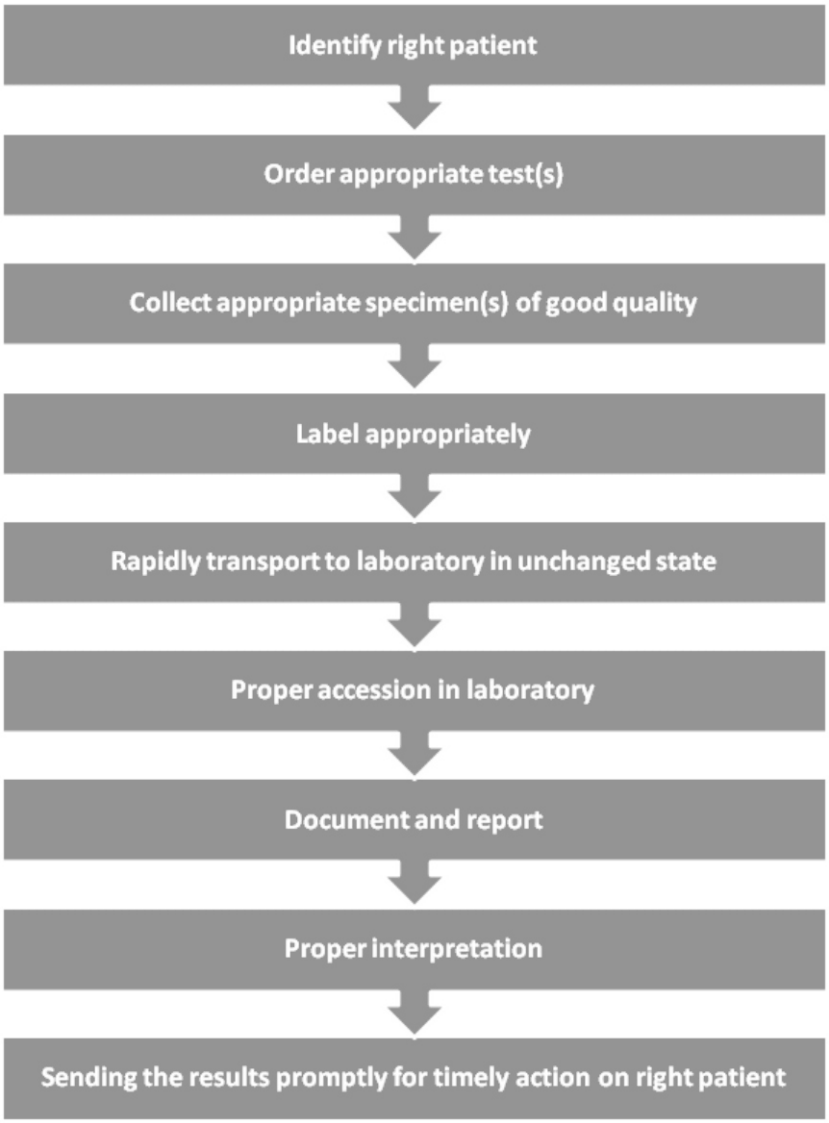


FIGURE 21-2. Algorithm of Quality Assurance in Clinical Microbiology

BIBLIOGRAPHY

Isenberg, H. Clinical Microbiology Procedures Handbook. Washington, DC: ASM press, 2016.
Mackie, T.J., Collee, J.G. McCartney, J.E. (1996) Mackie & McCartney Practical Medical Microbiology. New York; Churchill Livingstone.
Quality Assurance in Bacteriology and Immunology. 3rd Ed. World Health Organization (SEARO Regional Publication No. 47).

Chapter 22

Quality Control

Aamir Ijaz, Rehman Medical Institute, Peshawar; Muhammad Rafi Butt, MedAsk Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

Quality Control (QC) is a vital part of quality management, which is practiced in a clinical laboratory on daily basis and includes the comparison of laboratory results generated by one laboratory with numerous other laboratories around the world.

1. QC systems monitor the analytical process; detect and minimize errors during the analysis and prevent reporting of erroneous test results.
2. It is like 'product testing' in an industry
3. It can be used for quantitative data generated in Chemical Pathology, Hematology, Immunology and other sections of the laboratory. For such data statistical analysis, Westgard rules are applied.
4. QC procedures are also used for qualitative tests particularly those carried out in Microbiology, Hematology and Histopathology Departments.

TERMINOLOGY

Control Material

1. Quantitative tests - for substance that contains an established amount or concentration of analyte.
2. Qualitative tests - for substance that either contains or does not contain the analyte of interest.

Run

Batch of tests in which QC material has been included. It can be twice a day, weekly or monthly depending on the workload of the test.

TYPES OF QC

Internal: the purpose of internal QC is to ensure that the whole analytical system is running correctly. It is routinely run with each batch of samples and can be used to establish reference values for test analytes, or new reagent lots or shipments. QC procedures are necessary following instrument installation and repair to ensure the machine is functioning properly.

External (also called Proficiency Testing): External QC ensures that the values obtained by one laboratory are similar to those obtained by a different laboratory running the same testing procedure. It is a form of validating inter-laboratory performance

comparisons. Examples of proficiency testing programmes are National Quality Assessment Program Pakistan (NEQAPP), College of American Pathologists (CAP), Clinical Laboratory Improvement Amendments (CLIA) and Joint Commission International (JCI). For proficiency testing to be successful, it must be integrated within routine workload and analyzed by personnel who are running the tests and requires ongoing evaluation of results to for correction of unacceptable results.

CHOICE OF THE QC MATERIALS

The following needs to be considered when procuring QC materials:

a. Human or animal: The control matrix should be selected based on the expected patient population. For human laboratories, human QC materials are used that allow target values to be set closer to human medical decision limits; while, bovine, ovine or caprine may be optimal for use in veterinary laboratories.

b. Liquid or lyophilized: Liquid is better as there can be error in reconstitution of lyophilized material. Lyophilized on the other hand has the advantage of more basic storage requirements (room temp, longer expiration).

c. Assayed or un-assayed: Assayed are better as the target values are already set while for un-assayed one has to set target values as a first step.

The best material is human, liquid and assayed but this may be expensive. If there are financial constraints then one can go for bovine, lyophilized and un-assayed.

SOME BASIC STATISTICS

These statistical tools are useful for continuous data generated in Clinical Chemistry and some Haematology testing. In discrete and categorical data these tools are not used.

Gaussian/Normal Distribution

In a Gaussian distribution, all values are symmetrically distributed around the mean and form a characteristic “bell-shaped” curve. This distribution is assumed for all QC statistics.

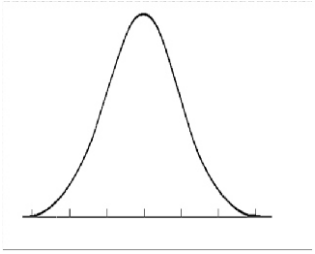


FIGURE 22-1: A typical Gaussian curve

Measures of Central Tendency

1. Mean ($\bar{x}$) - the mathematical average of a group of values, determined by adding a group of values (events) and dividing the result by the number of values (events).
2. Median - determined as the 'middle' of a group of numbers that have been arranged in sequential order i.e., there are equal numbers on either side of the 'middle' number. In odd # of observations, it is the middle observation; in even # of observations, it is the average of the two middle values.

3. Mode - the value that appears most frequently in a group of values. There can be more mode numbers, or none at all.

Standard Deviation (SD)

SD is a mathematical expression of the dispersion of a group of data around a mean. The greater the SD, the greater the poorer the precision is, so a smaller SD is desirable in QC results.

$$SD = \frac{\sqrt{\Sigma(x-\overline{x})}}{(n-1)}$$

Where:

n = number of observations (numerical values)

Σ = the sum of values i.e. differences between values and mean

x = the value of each individual observation

$\overline{x}$ = the mean value

Each of these values can be calculated for QC performed over time and plotted to determine whether the machine or test has been performing routinely. Having knowledge of previous QC values and comparison with new QC values will allow laboratory staff to determine when the machine needs a checking, maintenance or repair.

PROFICIENCY TESTING

Synonyms: External Quality Assessment Systems (EQAS)

Definition

"A system of objectively checking laboratory results by means of an external agency including comparison of a laboratory's result at intervals with those of other laboratories". The main objective is establishment of trueness.

OBJECTIVES OF EQA SCHEMES

Laboratory oriented objectives

Identifying possible deficiencies in laboratory practice, and guiding participants in any corrective actions to be taken for improvement; identifying the reliability characteristics of particular methods, materials and equipment and personnel under routine conditions and suggest corrective actions as appropriate; assessing and monitoring the impact of training; and help for the preparation of future trainings.

Public health-oriented objectives

Providing the basis for the comparability of results during epidemiological surveillance and disease control; collecting information on laboratory measurements (intra- and inter-laboratory) to alert professionals and/or government bodies about

problems related to traceability and harmonization of results and establish limits of acceptability of results as appropriate for a given purpose; and collecting information for the purpose of licensing or accreditation of laboratories.

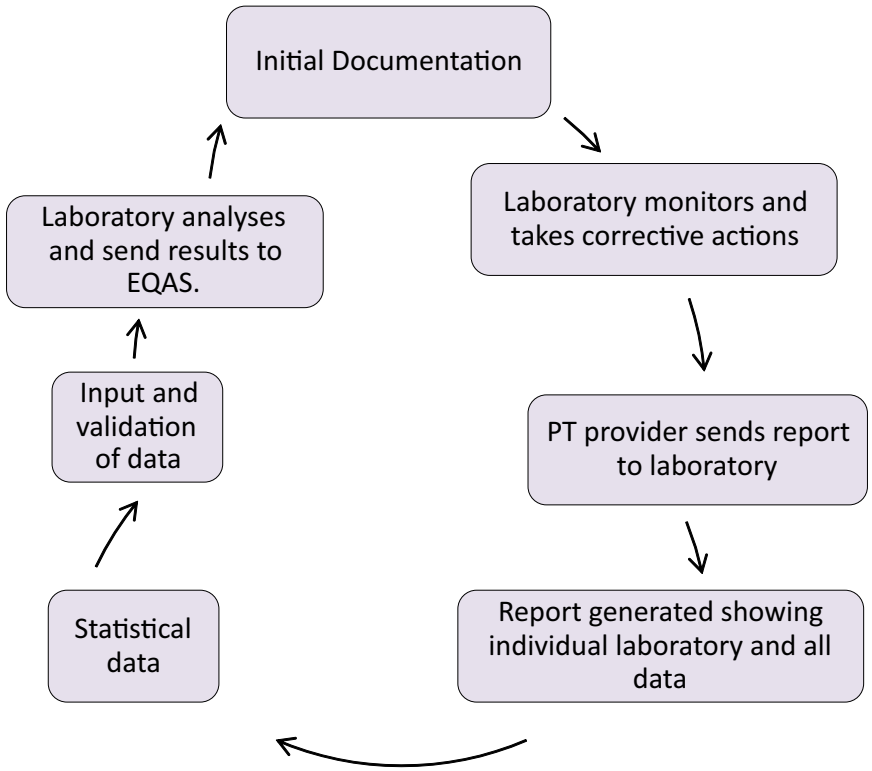


FIGURE 22-2: Components of a Typical EQAS Cycle

INTERNATIONAL EQAS AVAILABLE IN PAKISTAN

1. Randox External Quality Assessment Systems (UK) (www.randox.com/riqas-external-quality-assessment/).
2. Bio-Rad External Quality Assessment Systems (US) (www.bio-rad.com).
3. College of American Pathologists (US) (www.cap.org).
4. UK National External Quality Assessment Systems (UK NEQAS) (www.ukneqas.org.uk).
5. Regional External Quality Assurance Scheme of WHO in Microbiology (REQAS)

NATIONAL EXTERNAL QUALITY ASSURANCE PROGRAMME IN PAKISTAN (NEQAPP)

NEQAPP is being managed by Armed Forces Institute of Pathology (AFIP), Rawalpindi; specifically designed according to Pakistan's needs. It offers an economical option for establishing national quality goals in laboratories. The NEQAPP was started in 1996 and now has nearly 200 participating Pakistani laboratories. Programs are available for Chemical Pathology, Microbiology, Hematology and Histopathology.

BIBLIOGRAPHY

Burtis, C.A., Edward, R.A. (Eds) Teitz Textbook of Clinical Chemistry. 5th Ed. Saunders, W.B. Company; 2012; pp1403-1406.

CLSI/NCCLS. A quality management system model for healthcare; approved guideline - 2nd Ed. CLSI/NCCLS document HS1-A2. Wayne, PA, NCCLS, 2004.

Hilborne, L. Developing a core set of laboratory-based quality indicators. Presented at: Institute for Quality in Laboratory Medicine Conference, 29 April 2005, Atlanta, GA, US. Available at: http://cdc.confex.com/cdc/qlm2005/techprogram/paper_9086.htm.

Iqbal, S., Majid, H., Zubairi, M., Bhatti, N, Khan, N.F. Quality Management. In: Ijaz, A. Ed. Chemical Pathology for the Beginners. 1st Ed. Azeem Academy Lahore Pakistan. 2018:369-397.

ISO 15189:2007. Medical laboratories - particular requirements for quality and competence. Geneva: International Organization for Standardization, 2007.

ISO 9001:2000. Quality management systems - requirements. Geneva: International Organization for Standardization, 2000.

Kaplan, L.A., Pesce, A.J., Kazimieczak, S.C. (Eds) Clinical Chemistry; Theory, Analysis and Correlation. 4th Ed. Mosby Philadelphia, 2003; pp527.

Laboratory Quality Management System Handbook. World Health Organization 2011 (Online). Available at: http://www.who.int/ihr/publications/lqms_en.pdf.

Tools, Technologies & Training for Healthcare Laboratories. Westgard QC. (Online). Available at: https://www.westgard.com/mltirule.htm.

Chapter 23

Occurrence Management

Aamir Ijaz, Rehman Medical Institute, Peshawar; Muhammad Rafi Butt, MedAsk Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

The term 'Occurrence' will be used in this chapter to describe any event, which may directly or indirectly effect patient-care in a clinical laboratory setting. Laboratory errors are the most important type of occurrence encountered by a laboratory person. We will discuss various modalities of handling these errors and mechanisms to prevent them.

This chapter will encompass following topics:

- Laboratory errors
- Principles of trouble shooting
- Delta Check

LABORATORY ERRORS

Pre-analytical Errors

Errors in the first phase of laboratory process are much more common than analytical errors. These errors can result from specimen collection, handling and processing, physiological variables such as the effect of lifestyle, age, gender, pregnancy and menstruation, endogenous variables such as drugs etc., Patient identification errors, phlebotomy technique, test collection procedures, specimen transport, specimen processing are other examples of pre-analytical errors

Pre-analytical errors cannot be detected by routine internal quality control or external quality assessment procedures. One way of detecting these errors is Delta Check, this will be discussed as a separate topic in this chapter.

Types of Analytical Errors

Random Error: Imprecision of the test system causing a scatter or spread of control values around the mean. Some causes of random error include: air bubbles in reagent, improperly mixed reagents, reagent lines, sampling, or reagent syringes, improperly fitting pipette tips, clogged or imprecise pipettes, or fluctuations in power supply.

Systematic error: Systematic change in the test system resulting in a displacement of the mean from the original value. Systematic error of an analytic system is predictable and causes shifts or trends on control charts that are consistently low or high. Some causes of systemic errors include: change in reagent or calibrator lot numbers, wrong calibrator values, improperly prepared reagents, deterioration of reagents or calibrators, inappropriate storage of reagents or calibrators, variation in specimen or reagent volumes

due to pipettor misalignments, variation in temperature or reaction chambers, deterioration of photometric light source or variation in procedure between technologists.

DIFFERENCE BETWEEN PRECISION AND ACCURACY

Precision: The ability to get the same (but not necessarily 'true') result time after time. The degree of fluctuation in the measurements is indicative of the imprecision of the assay.

Accuracy: The closeness of measurements to the true value is indicative of the accuracy of the assay. An accurate result is one that is the 'true' result.

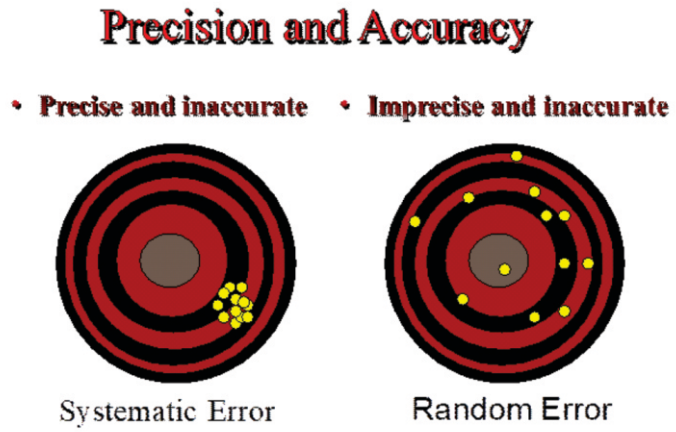


FIGURE 23-1: Concept of Errors with reference to Precision and Accuracy

SHIFT AND TREND

Shift: QC data results are distributed on one side of the mean for 6-7 consecutive days (Fig 22-2). Causes of shift can include: inaccurate calibration/recalibration, sudden failure or change in the light source, change in reagent formulation, change of reagent lot, sudden change in incubation temperature (enzymes), failure in the sampling system, or failure in reagent dispense system.

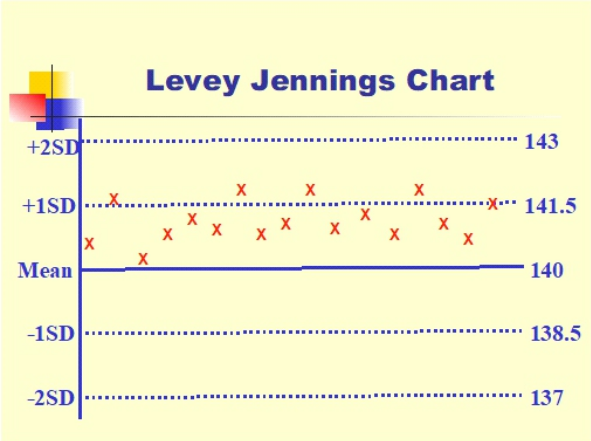


FIGURE 23-2: An example of Shift

Trend: Consistent increase or decrease of QC data points over a period of 6-7 days (Fig 22-3). Causes include: gradual deterioration of control materials, deterioration of the instrument light source, gradual accumulation of debris in sample/reagent tubing, aging of reagents, gradual deterioration of incubation chamber, or gradual deterioration of light filter integrity.

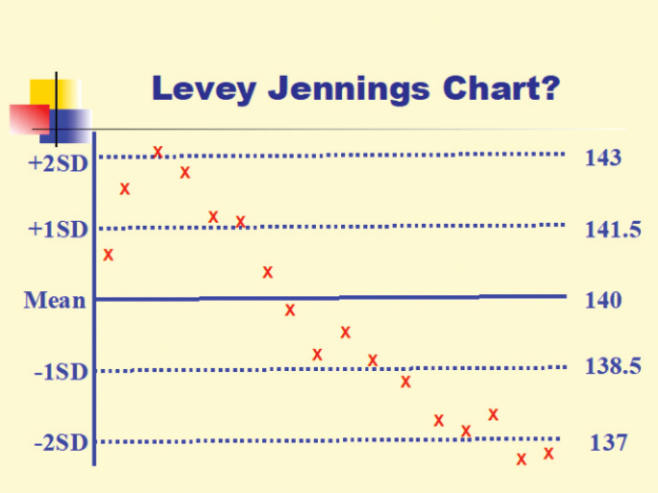


FIGURE 23-3: An example of Trend

PRINCIPLES OF TROUBLE SHOOTING

Detection and Resolution of Quality Problems

Testing system is considered out of control if validity of results is not appropriate. Criteria for out of control decision include:

- Laboratory director or technical supervisor declares system out of control.
- Control values exceed predetermined control limits.
- The method is said to be out of control if it has inappropriate interference which is not correctable immediately.
- If there is unacceptable imprecision, nonlinearity or interferences.
- If individual patient result exceeds delta check against previous results.

Actions to bring a testing system back into control

One at a Time Principle: When an error is detected in a QC System, it is important to follow the principle of "One at a Time". If all the steps given below are changed together, the real root cause of error will not be found (Fig 22-4).

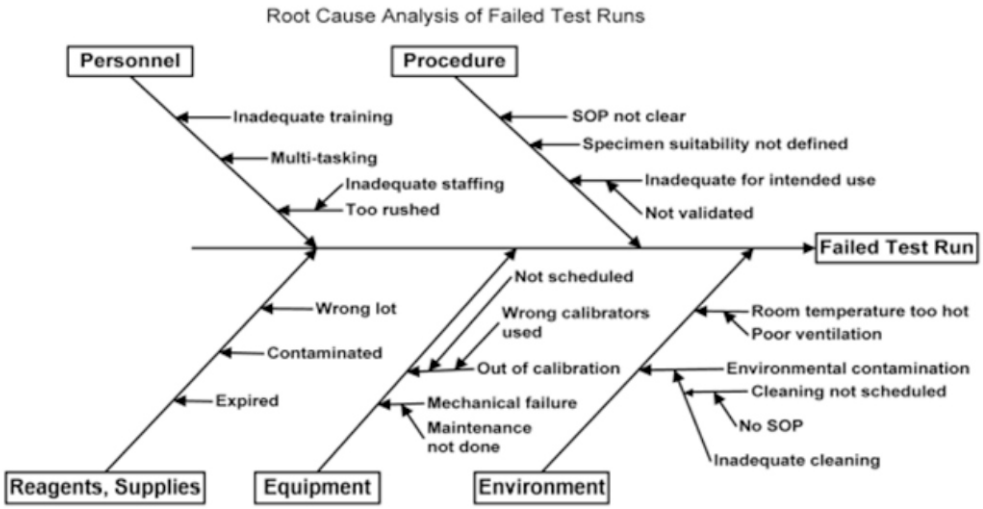


FIGURE 23-4. Consideration in an occurrence of failed test

Steps for Trouble Shooting:

- Repeat assays on control specimens using fresh aliquots of QC pool.
- Repeat assay on control specimen using newly constituted set of control.
- Look for problems like clots, reagent levels, mechanical fault.
- Recalibrate the instrument for out of control analyte and re-assay all controls.
- Install new bottle or new lot for one or all reagents, recalibrate and re-assay all controls.
- Perform periodic maintenance, recalibrate and re-assay all controls.

Strategy to be Adopted for QC:

- If any of these responses result in acceptable QC data, only then patients result can be released.
- No more than 15-20 minutes should be spent in problem solving before notifying supervisors.
- Assay different control materials of similar known concentration to find the fault of original control material.
- Call manufacturer to determine the cause, follow manufacturer's instruction and then re-assay all controls.
- After servicing of instrument by manufacturer recalibrate and re-assay all controls.
- Use accuracy-based materials to evaluate quality specification of analytical system by checking:
    - Linearity
    - Accuracy
    - Bias
    - Precision
    - Analytical sensitivity
    - Minimal detectable change

- Determine whether testing system has changed by re-evaluating reference interval.
- Consult director or technical supervisor to declare method out of control if above steps fail.
- Final action involves replacement of method or instrument with one that allows laboratory to meet its medical or proficiency goals.

Documentation

QC record should include maintenance of log book for every analyte and for every instrument. All the occurrence should be recorded as:

- Date
- Name of analyte
- Complete testing system including:
    - Source of reagent
    - Instruments
    - Calibrators
    - Controls
- Description of problem
- Problem resolution
- Name of staff
- Final actions

Procedure to follow during Testing System Failure:

Out of control conditions can constitute a laboratory emergency which can be managed as follows:

- Use suitable back up method
- Sending test to reference laboratory
- Temporarily discontinuing the test
- Laboratory policy should define how much time the technologist can spend trouble shooting a method before using alternate system

DELTA CHECK

Introduction

First described in 1974, Delta Check compares the current test result with a previous result from the same test obtained over a short period of time (within 96 hours) for the same patient. Addresses errors that are not detectable with other methods of QC. If the change in the value of the analyte exceeds an expected physiological range, the result is flagged as a possible error.

Delta Check Alert

A “Delta Check” failure or alert occurs if there is a discrepancy in the patient results; when the difference between a patient's present lab result and their previous result exceeds a predefined limit within a predefined length of time.

Why Using Delta Checks?

Delta checks are useful quality improvement measures that can help the lab identify possible patient-specific errors e.g.

- Early error identification has considerable implications for patient-care and safety. Deadly errors e.g. incorrect drug dosing, anticoagulation therapy, cardiac intervention, blood transfusion, etc. from erroneous lab results.
- Predictive value for detecting true specimen errors is between 0.4 and 6%.
- Studies have found that the majority of delta check failures (>75%) can be attributed to true changes in the patient's medical condition.
- Providers need to be alerted to large biological variation in their patients and may indicate need for intervention.

Main Goals

Delta checks are useful quality improvement measures that can help the lab identify possible patient-specific errors. There are two main goals:

- Identification of test quality issues or patient identification problem.
- Detection of changes in patient's condition or disease state.

Causes of Delta Check Alert (Discrepant Results)

Causes of the discrepant results giving rise to delta check failure are patient specific, numerous and can be grouped into pre-analytical, analytical and post analytical. Examples include:

- Majority of our investigative power lies in detecting the analytical variation (QC, imprecision, bias).
- The analytical variation can be instrument specific or method specific. For example, variations due to issues in instrument can be due to probe and pipette errors, variation in reagent volumes, air bubbles and calibration. While method specific issues leading to variation could be due to errors in dilution, improper mixing, pH, temperature, reagent and lot changes.
- Main goal of the human body is homeostasis. The body attempts to keep essential analytes from fluctuating on a daily basis. There are rhythmic changes.
- Changes over the life span and delta check limits may change with patient age. Life style changes cause variation in the nutritional status and changes in the activity level.
- Treatments and medical intervention may cause large fluctuations in overall patient biology, affecting a variety of test results, like intravenous fluids, total parenteral nutrition (TPN), chemotherapeutics, dialysis, organ transplantation and other medicines.

Auto Verification (AV) Systems

Central laboratories deal with an enormous number of tests each day and are always under pressure to increase service quality, simplify processes, decreasing the report release Turn Around Time (TAT). So, the process of Delta Check has been automated. In an AV system, the verification rules and the criteria of the test results are built into the middleware, so instead of the results requiring a manual check, they are auto-verified by the computer.

With an AV system, at least 80% of the test reports can be auto-verified without the need of manual intervention, thereby allowing medical technologists to concentrate on the test reports intercepted in middleware. Test reports are auto-verified by the medical technologist against report check rules on the Laboratory Information System (LIS) or middleware. These verifications include:

- Limit check rules
- Critical values
- Comparison with former results
- Consistency of related results
- Limit check rules
- Critical values
- Comparison with former results
- Consistency of related results

BIBLIOGRAPHY

Cembrowski, G.S., Carey, R.N. Laboratory Quality Management: QC and QA, ASCP Press (1989).

Cooper, G., and Gillions, T. Producing Reliable Test Results in the Medical Laboratory (2007).

Davies, O.L., Goldsmith, P.L. Statistical Methods in Research and Production. New York (1984).

Howanitz, P.J., and Joan H. Laboratory Quality Assurance. McGraw-Hill Book Company (1987).

Iqbal, S., Majid, H., Zubairi, M., Bhatti, N, Khan, N.F. Quality Management. In: Ijaz, A. Ed. Chemical Pathology for the Beginners. 1st Ed. Azeem Academy Lahore Pakistan. 2018:369-397.

Kaplan L.A., Pesce A.J. In: Theory, Analysis, Correlation Clinical Chemistry. 5th Ed. pp470-473.

National Committee for Clinical Laboratory Standards. Internal Quality Control: Principles and Definitions; C-24A.

Weisbrot, M.D. Statistics for the Clinical Laboratory. J.B. Lippincott Company, Philadelphia (1985).

Westgard, J.O., Barry, P.L., Hunt M.R., Groth, T. A Multi-Rule Shewhart Chart for Quality Control in Clinical Chemistry; Clin Chem. 1981; 27(3): 493-501.

Westgard, J.O. et al. Combined Shewhart - CUSUM Control Chart for Improved Quality Control in Clinical Chemistry; Clin Chem. 1977; 23(10): 1881-1887.

Westgard, J.O., Koch, D.D., Oryall, J.J., Quam, E.F., Feldbruegge, D.H., Dowd, D.E., Barry, P.L. Selection of Medically Useful Quality Control Procedures for Individual Tests Done in a Multi-Test System; Clin Chem. 1990; 36: 230.

Chapter 24

Method Validation

Aamir Ijaz, Rehman Medical Institute, Peshawar; Ayesha Junaid, Shifa College of Medicine, Islamabad; Muhammad Rafi Butt, MedAsk, Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

INTRODUCTION

Method validation is the process to determine how much any potential error might be present in a test result produced by a method in the laboratory. Laboratory personnel should also determine the amount of error, that will not affect the interpretation of the test result and compromise patientcare. If the observed errors are enormous so as to cause an incorrect interpretation, the method isn't acceptable. To be acceptable, the observed errors need to be small relative to changes that will cause a change in the interpretation of a test result.

TERMINOLOGY

Method Evaluation: Method evaluation is a detailed process in which larger number of characteristics is needed to establish or evaluate method characteristics of an untested method. Highly complex methods should be studied more thoroughly. Any methods that are modified or developed by the laboratory itself must be evaluated extensively.

Method Validation: Method validation requires less vigorous process as the method is already well tested. Most moderately complex methods have been well studied by manufacturers as part of their own development process; therefore, the laboratory can perform less extensive studies to validate method performance.

Method Verification: Method verification is the confirmation by examination and provision of objective evidence that the particular requirements have been fulfilled. It is verification of the claims of the manufacturer and may consist of just one to two trials e.g. verification of SD.

CHARACTERISTICS TO BE CONSIDERED FOR SELECTION OF A ROUTINE TEST

Application Characteristics

Application characteristics are factors that determine whether a method can be implemented in a particular laboratory situation or not. It includes:

- The type of specimen
- Volume of specimen
- Workload appropriate for the testing situation (high volume centralized lab vs. low volume point-of-care)

- Cost per test
- Turnaround time for analysis
- Operator skills
- Operator training requirements

Methodology Characteristics

Method characteristics are factors, which, in principle, should contribute to best performance. In general, these are concerned with the analytical sensitivity and specificity of the method of testing. It includes:

- The type of standards
- Traceability of standard
- Assigned values
- Chemical principle
- Reagents
- Reaction conditions
- Measurement principle
- Measurement capabilities

Performance Characteristics

Performance characteristics are factors, which, in practice, demonstrate how well a method performs. It includes:

- Accuracy
- Sensitivity
- Analytical measurement range
- Linearity
- Recovery
- Precision
- Detection limit
- Selectivity /Specificity of the method
- Robustness
- Reliability (Accuracy + Precision)

Accuracy: It is the closeness of the analytical value to the 'true value'

Bias: This is a measure of the difference between the expected test result and the accepted reference value due to systematic method and laboratory error. It is expressed as a percentage.

Precision: This is the scatter of the values around a central tendency. Following three parameters describe precision:

- **Repeatability:** Repeatability expresses the precision under the same operating condition under a short interval of time. It is also termed intra-assay precision.
- **Reproducibility:** Reproducibility expresses the precision between laboratories (collaborative studies usually are applied to standardization of the methodology).

- **Intermediate Precision:** Intermediate precision expresses within-laboratories variations, like different days, different analysts, different equipment.

Recovery: Detection of a known amount of an analytical parameter added in a specimen. It is a measure to estimate accuracy by analyzing samples spiked at three different concentrations (low, medium, high) covering the working range.

Linearity and Range: The linearity of a method is its ability to elicit results that are directly, or by a well-defined mathematical transformation, proportional to the concentration of analyte in the sample. Analytical measurement range (AMR) of the method is the area between the lower and the upper limits of quantitation that is also linear. Within AMR of the method, results are accurate, precise and "linear". (Figure 23. 1)

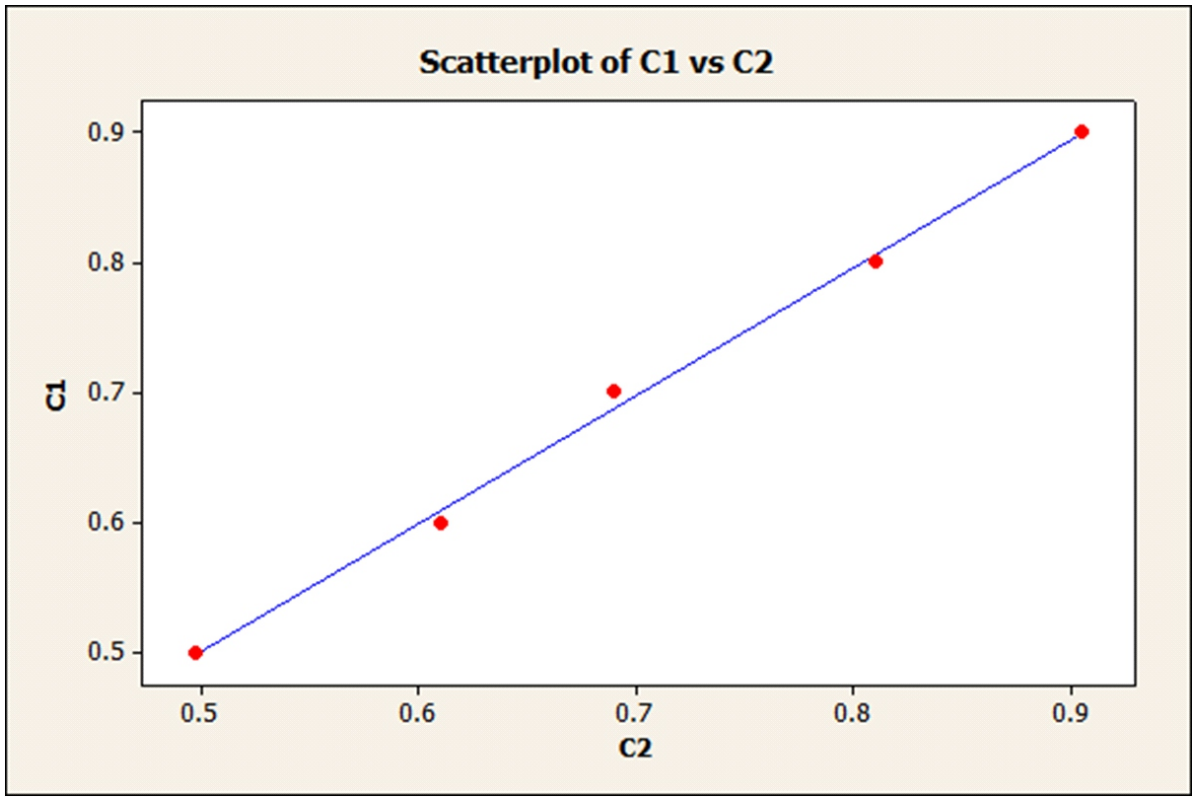


FIGURE 24-1: A typical Linearity Plot

Limits of Detection (LOD): The limit of detection of a method may be defined as the concentration of an analyte which initiates a signal that is significantly different from the blank. The LOD is the lowest concentration of the analyte that can be distinguished from background. The results obtained at the LOD are not necessarily precise or accurate.

Limits of Quantitation (LOQ): The limits of quantitation are the lowest and the highest concentrations of an analyte in a sample or specimen that can be measured with an acceptable level of (uncertainty) accuracy and precision.

Robustness/Ruggedness: The degree of independence of the method of analysis from minor deviations in the experimental conditions of the method of analysis. It is also an indicator of degree of reproducibility.

Analytical Sensitivity: This is the change in the analytical response divided by the corresponding change in the concentration of a standard (calibration) curve, i.e., the slope of the analytical calibration curve. A method is said to be sensitive if a small change in concentration of the analyte causes a large change in the analytical measurement. Analytical sensitivity actually determines the gradient of the calibration curve.

Analytical Specificity: Specify those substances which might be expected to give rise to an interfering signal. A check for random interferences should be performed by analysis of a set of representative blank samples. Indicates the extent to which the method can distinguish between the analyte of interest and interfering substances.

LABORATORY STUDIES REQUIRED FOR METHOD VALIDATION

When performance characteristics of a new method has to be validated in a laboratory, following studies are carried out:

Replications Studies: A minimum of 20 specimens should be measured in the time period of interest. A larger number of specimens will give a better estimate of the random error. Statistical calculations used in the replication studies include mean, Standard Deviation (S) and Coefficient of Variation (CV) (Please see Chapter 21 for details).

Interference Study: It is carried out to detect Constant Systemic Error. Factors contributing to constant error are independent of analyte concentration, caused by an interfering substance in all specimens or in reagents that initiates a false signal. Examples include improper blanking of samples or the reagents; reaction between interfering substance and the reagent; and substance interfering in the reaction between reagent and analyte. Interfering substance may also inhibit or destroy the reagent, so it remains in suboptimal amount for the reaction with analyte. Interfering conditions include hemolysis, lipaemia, icterus, related compounds, drugs, dietary substances, sample additives etc.

Recovery Study: A recovery study is carried out to detect Proportional Systemic Errors i.e., an error that is in one direction and which increases (or decreases) with changing concentrations of the analyte. It is most often caused by incorrect assignment of the amount of substance in the calibrator. If the calibrator has more analyte than is labeled (120 mg/dl glucose instead of 100 mg/dl as labeled on calibrator), all unknown determinations would be low, and vice versa.

Comparison of Methods Study (The Mother of Experiments): This experiment is carried out on actual patient specimens with various concentrations of the analyte. Minimum 40 specimens are tested using the method to be evaluated and a reference method (or comparative method). The experiment should span over a period of 5 days. At the end of analyses, following statistics are applied:

- Bias
- Correlation study

- Independent sample 't' test
- Linear Regression
- Bland Altmann plot

Transference of a Reference Values: New reference values are calculated based on the systematic analytical differences between the two methods. It should be verified by running at least 20 specimens. It should be done only if the lab has previously established reference values and is changing the methodology. It is an acceptable, but not recommended method. To reduce errors introduced by drift, transference calculations should be limited to one method change.

BIBLIOGRAPHY

American Association of Clinical Chemistry. Publication on Method Valuation. Available at: https://www.aacc.org/.

International Organization of Standardization. Medical Laboratories. Particular requirements of quality and competence (15189). Geneva: ISO, 2007. Available at:
https://www.aacc.org/-/media/Files/Meetings-and-Events/Resources-from-Past-Events/Conferences/2013/Professional-Practice/April-28/MV_Method_Validation_Apr_28_2013.pdf?

Kaplan, L.A. and Pesce, A.J. Evaluation of Methods. In: Kaplan, L.A., and Pesce A.J., Eds. Clinical Chemistry: Theory, Analysis, Correlation. 5th Ed. MOSBY (Elsevier). 2010:480-506.

Linnet, K. A review on the methodology for assessing diagnostic tests. Clin Chem. 1988;34:1399-86.

Linnet, K., and Boyd, J.C. Selection and Analytical Evaluation of Methods - with Statistical Techniques. In: Burtis, C.A., Ashwood, E.R., and Bruns, D.E. (Eds). Teitz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th Ed. Saunders (Elsevier). Philadelphia, US. 2012:7-9.

Magnusson, B., and Örnemark, U. (eds.) Eurachem Guide: The Fitness for Purpose of Analytical Methods – A Laboratory Guide to Method Validation and Related Topics. 2nd Ed. (2014). ISBN 978-91-87461-59-0.

Supplementary guidelines on good manufacturing practices: validation. WHO Technical Report Series, No. 937, 2006.

Chapter 25

Laboratory Certification & Accreditation

Aamir Ijaz, Rehman Medical Institute, Peshawar; Ayesha Junaid, Shifa College of Medicine, Islamabad; Muhammad Rafi Butt, MedAsk, Rawalpindi; Brian Lubbers, Kansas State Veterinary Diagnostic Laboratory

In this chapter, we will briefly present an introduction to the significance and processes involved in laboratory accreditation.

CERTIFICATION VS ACCREDITATION

Certification is used for verifying that personnel have adequate credentials to practice certain disciplines, as well as for verifying that products meet certain requirements.

Accreditation is used to verify that the laboratories have an appropriate quality management system and can properly perform certain test methods and calibration parameters according to their scopes of accreditation. Any laboratory conducting medical testing is eligible to apply for the accreditation program.

ACCREDITATION OF CLINICAL LABORATORIES (MEDICAL AND VETERINARY)

Medical laboratories are a critical part of the healthcare system. To improve the accuracy of results, medical labs around the world have begun adopting ISO 15189: Medical laboratories - requirements for quality and competence. The standard requires the clinical labs to implement a quality management system. This requires them to document all their processes and procedures to ensure lab technologists understand and follow the correct method when conducting a test.

WHY ACCREDITATION?

There are number of reasons why a medical laboratory may seek recognition as being compliant with standards. In some cases, a laboratory is legally mandated or contractually mandated to achieve accreditation to serve as a national or regional reference laboratory. For other laboratories, achieving accreditation helps to increase the competitiveness of the laboratory. Achieving accreditation ensures to outside parties that the laboratory is functioning in accordance with accepted norms.

ACCREDITATION INITIATIVE AT NATIONAL LEVEL

A laboratory accreditation initiative within a country requires at least 3 elements:

- A laboratory policy framework that makes accreditation a requirement for laboratories.
- Designated quality standards against which laboratories can be assessed.
- Accrediting bodies (local or international) authorized to assess the laboratories and certify their performance against the designated quality standards.

ACCREDITATION BODIES

Pakistan National Accreditation Council (PNAC)

This council works under the auspices of Ministry of Science & Technology, Government of Pakistan. PNAC has accredited a few laboratories in Pakistan e.g. AFIP Rawalpindi, Chughtai Lab Lahore, Islamabad Diagnostic.

Joint Commission International (JCI), US, & College of American Pathologists (CAP)

These are international bodies, which carry out detailed assessments for grant of accreditation. Presently only one laboratory in Pakistan has received CAP accreditation i.e., AKU Hospital Karachi. Shifa International Hospital Lab is a participant of CAP surveys for most of the test menu of the laboratory sections but is not yet accredited. Shaukat Khanum Lab is also in process.

ACCREDITATION STANDARDS

ISO 15189 is a globally recognized standard that has been specifically created for medical laboratories to help them develop their quality management systems and assess their competence.

ISO 17025 is for laboratories not involved in clinical work e.g. calibration labs or forensic sciences labs.

PROFICIENCY TESTING (PT) IS A MUST FOR LAB ACCREDITATION

Participation in PT programs, a key component of accreditation, leads to more accurate test results. Repeated PT participation improves laboratory results and minimizes outlying test parameters. Adherence to such quality standards and participation in accreditation programs can improve operational efficiency and customer service and reduce rates of laboratory errors.

The variability of test results and the frequency of errors can be reduced by implementing and monitoring a comprehensive laboratory quality management system. Accreditation provides verification that laboratories are adhering to established quality and competence standards deemed necessary for accurate and reliable patient testing and the safety of the staff and environment.

ACCREDITATION IS RECOGNITION

Laboratories that achieve accreditation are recognized for superior test reliability, operational performance, quality management and competence. Accredited laboratories can become more accountable and less dependent on external support. In addition, efforts made to achieve accreditation may also lead to improvements in the management of laboratory networks by focusing attention on areas of greatest need and accelerating improvement in areas such as supply chain, training, and instrument maintenance.

INITIATIVE FOR ACCREDITATION

Accreditation initiatives also strengthen:

- Laboratory policy updates
- Long-term strategic planning

- Procurement and supply chain systems
- Laboratory networking
- Human resources management and training
- Instrument service maintenance
- Data and quality management

ISO 15189 OVERVIEW

The ISO 15189 standard, designed specifically for medical laboratories covers 15 management requirements and 8 technical requirements.

ISO 15189:2012 Medical Laboratories - Requirements for Quality and Competence

Several requirements for achieving ISO 15189 compliance are listed below. Complete requirements can be found online: https://www.iso.org/standard/56115.html.

Management Requirements: (Clause 4)

4.1 Organization and management responsibility: The laboratory or the organization of which the laboratory is a part shall be an entity that can be held legally responsible for its activities.

4.2 Quality management system: The laboratory shall establish, document, implement and maintain a quality management system and continually improve its effectiveness in accordance with requirements of this international standard. The quality management system shall provide for the integration of all processes required to fulfil its quality policy and objectives and meet the needs and requirements of the users.

4.3 Document control: The laboratory shall control documents required by the quality management system and shall ensure that unintended use of any obsolete document is prevented.

4.4 Service agreements: The laboratory shall have documented procedures for the establishment and review of agreements for providing medical laboratory services.

4.5 Examination by referral laboratories: The laboratory shall have a documented procedure for selecting and evaluating referral laboratories and consultants who provide opinions as well as interpretation for complex testing in any discipline.

4.6 External services and supplies: The laboratory shall have documented procedures for the selection and purchasing of external services, equipment, reagents and consumable supplies that affect the quality of its services (see also 5.3).

4.7 Advisory services: The laboratory shall establish arrangements for communicating with users on the following:

- Advising on choice of examinations and use of the services, including required type of sample, clinical indications and limitations of examination procedures, and the frequency of requesting the examination
- Advising on individual clinical cases
- Professional judgements on the interpretation of the results of examinations
- Promoting the effective utilization of laboratory services

- Consulting on scientific and logistic matters such as instances of failure of sample (s) to meet acceptance criteria.

4.8 Resolution of complaints: The laboratory shall have a documented procedure for the management of complaints or other feedback received from clinicians, patients, laboratory staff or other parties. Records shall be maintained of all complaints and their investigation and the action(s) taken.

4.9 Identification and control of nonconformities: The laboratory shall have a documented procedure to identify and manage nonconformities in any aspect of quality management system, including pre-examination, examination and post-examination processes.

4.10 Corrective action: The laboratory shall take corrective action to eliminate the cause(s) of nonconformities. Corrective actions shall be appropriate to the effects of the nonconformities encountered.

4.11 Preventive action: The laboratory shall determine action to eliminate the causes of potential nonconformities in order to prevent their occurrence. Preventive actions shall be appropriate to the effects of the potential problems.

4.12 Continual improvement: The continual improvement of the laboratory processes is essential in a quality management system. This process is applied to all procedures and processes that are a part of the path of workflow in laboratory.

4.13 Control of records: The laboratory shall have a documented procedure for identification, collection, indexing, access, storage, maintenance, amendment and safe disposal of quality and technical records. Records shall be created concurrently with performance of each activity that affects the quality of the examination.

4.14 Internal audit: The laboratory shall conduct internal audits at planned intervals to determine whether all activities of the quality management system, including pre-examination, examination and post-examination conform to the requirements of this international standard and to requirements established by the laboratory, and are implemented, effective and maintained.

4.15 Management review: Laboratory management shall review the quality management system at planned intervals to ensure its continuing suitability, adequacy and effectiveness and support of patient care.

Technical Requirements (Clause 5)

5.1 Personnel: Personnel qualifications documentation, job descriptions, personal introduction to the organizational environment program, training provision, competence assessment per person, reviews of staff performance, continuing education and professional development, and personal records of relevant skills.

5.2 Accommodation and environmental conditions: Laboratory and office facilities to provide an environment appropriate for the duties to be undertaken, storage facilities, staff services, patient sample collection facilities, facility maintenance and environmental conditions.

5.3 Laboratory equipment, reagents, and consumables:

- Equipment: Documented procedure, acceptance testing, instructions for use, calibration and metrological traceability, maintenance and repair, adverse indented reporting, and records.

- Reagents and consumables: Documented procedure, reception and storage, acceptance testing, inventory management, instructions for use, adverse incident reporting, and records.

5.4 Pre-examination processes: Documented procedures, information for patients and users, request form information, first sample collection and handling, sample transportation, sample reception, pre-examination handling, preparation, and storage.

5.5 Examination procedures: Examination procedure selection which has been validated for their intended use, verification of analysis procedures, validation of test methods, measurement uncertainty of measured quantity values, biological reference intervals or clinical decision values, and documentation of testing procedures.

5.6 Ensuring quality of examination procedures: Quality control procedures design to verify the attainment of the intended quality of results, quality control materials, quality control data, inter-laboratory comparisons, analysis of inter-laboratory comparison samples, evaluation of laboratory performance, and comparability of examination results.

5.7 Post-examination procedures: Review of results, storage, retention, and disposal of clinical samples.

5.8 Reporting of results: Report of examination results, the report attributes, and content.

5.9 Release of results: Documented procedures, automatic selection and reporting of results, and revised reports.

5.10 Laboratory information management: Authorities and responsibilities, and information system management.

DOCUMENTATION OF THE SYSTEM

Documenting all policies and procedures used in the laboratory facility is important for a certification process. Remember that documentation should reflect, “Say what you do; do what you say”.

Working closely with those who perform the functions, you must carefully document everything you do in a set of processes and procedures. Once they are documented, you must ensure all staff understand and follow these processes and procedures. They must know where to find them and the documents must be controlled i.e., the documents should be properly numbered and archived under the supervision of managerial staff, so staff are always looking at the most recent version and not following previous procedures.

There are four levels of documentation: policies, processes, procedures, and records.

Policies

Policies are statements that describe what is done and why. Rationalization of the policies cannot be overemphasized and logically explained. They define goals, and briefly state intent and direction. They will form the basis of the quality manual and are high-level looks at topics such as personnel, inventory control, document control, strategic planning, etc.

Policies and procedures should reflect what an organization actually does - not wish - for attaining outcomes or goals. Auditors will look for the evidence that policies and procedures reflect reality, not desires.

Processes

A process is a series of interrelated steps involved in an activity that uses resources and is managed to transform inputs into outputs. Processes are usually documented in the form of a flowchart, and not as step-by-step instructions.

Procedures

Procedures are the detailed step-by-step instructions that convey the employees how to perform an activity, examination, or step in a process. It is essential to document not only technical instructions but other activities as well, such as how to respond to a complaint by a laboratory customer, instructions on how to use the IT system, and how to validate equipment before use. The documentation provides workers with transparency and clarification.

Records

Records are anything that provides evidence. It is a history of what was done and cannot be changed. Examples of records include a filled-out or completed form, examination results and reports, and instrument printouts.

COMMON MISTAKES WHILE DOCUMENTING SYSTEMS

- Document technical procedures only, but not management activities, such as the training and orientation of new employees and performance evaluation.
- Hire a consultant to write procedures or purchase a commercial package of pre-written policies. Such packages may not reflect what they do. Those who actually perform an activity must play a key role in documenting the processes and procedures.

HOW TO GET ACCREDITED

In general, the laboratory must be a registered legal entity and has the intent to seek accreditation. The laboratory director should appoint a person to oversee application for accreditation. This person should work to make sure all personnel are onboard with the accreditation process and all information is properly conveyed to the accrediting body.

Depending on the accreditation body, procedures may be different. However, in general, the accrediting body would like to see all documentation from the laboratory, perform an inspection, and conduct audits of all laboratory records. It is best to contact and work with the accrediting body prior to applying for accreditation to ensure that the process is well understood, and the correct paperwork is submitted.

BIBLIOGRAPHY

Carling, R. A practical guide to ISO 15189 in laboratory medicine. Ann Clin Biochem. 2014; 51: 720.

Ijaz. A., Khan, F.A., Dilawar, M. Laboratory Accreditation: Editorial. Pak J Pathol. 2004;15(1):1-2.

Iqbal, S., Ijaz. A., Sharafat, S. Estimation of uncertainty measurement - A prerequisite of ISO1589 accreditation for clinical laboratories. J Pak Med Assoc. 2017:67;701-705.

ISO 15189:2012 Medical laboratories - Requirements for quality and competence. Available at: https://www.westgard.com/iso-15189-2012-requirements-1.htm.

Klee, G.G., Westgard, J.O. Quality Management. In: Burtis, C.A., and Bruns, D.E. Eds. Tietz Fundamentals of Clinical Chemistry & Molecular Diagnostics. 5th Ed. Saunders (Elsevier). Philadelphia, US. 2012:177.

Management Requirement of ISO 15189:2012. Available at: www.ec.europa.eu/enlargement/taiex/dyn/create_speech.jsp?speechID=345.

Munir, M.U., Ijaz, A. National External Quality Assurance Program Pakistan (NEQAPP) - a milestone in proficiency testing in Pakistan. eJIFCC. 2016;27(4):344-50.

Nkengasong, N. Strengthening laboratory services and systems in resource-poor countries [editorial]. Am J Clin Pathol. 2009;131:774.

Pakistan National Council for Accreditation (PNAC). Medical Laboratory Accreditation (ISO-15189:2012). Available at: http://pnac.org.pk/medical-laboratories-accreditation-iso-15189/.

Peter, T.F., Rotz, P.D., Blair, D.H., Khine, A.A., Freeman, R.A., Murtagh, M.M. Impact of laboratory accreditation on patient care and the health system. Am J Clin Pathol. 2010;134:550-555.

Appendix 1

Units of Measure

Faisal Hanif, Bahria University Medical College; Umar Khurshid, Armed Forces Institute of Pathology, Rawalpindi

Health professionals and patients are usually baffled by the diversity of the units in which individual laboratory results are reported. Though any valid reporting unit is used; care-givers either don't know about the conversion factors or else are too busy to engage in mathematical conversions, on one hand, while patients seem to be at a total loss as how to chart the progress of a particular test over a period of time in which different reporting units have been employed. Hence most importantly it leads to patient dissatisfaction and concern, apart from the requirement by the care-giver to interpret the result correctly and precisely.

The following table offers the latest reporting units and their abbreviations:

Parameter unit	**Suggested abbreviation**
Centimeter	Cm
Copies /microliter	Copies/mcL
Copies per milliliter	Copies/ mL
Day(s)	d
Deciliters	dL
Degrees measured	degrees
Degrees Celsius	deg C
Events	Events
Femtoliters	fL
Gram(s)	g
Grams per deciliter	g/dl
Haemoglobin	Hb
Hour(s)	h
International units	IU
International units/liter	IU/L
International units per deciliter	IU/dL
Kilograms	Kg
Liter	L
Microinternational units	mcIU
Micrograms	Mcg
Micrograms per deciliter	mcg/dL
Microliters	mcL
Microunit	mcU
Micromoles per liter	mcmol/L

Parameter unit	Suggested abbreviation
Micromoles per liter	mcmol/L
Millimoles per liter	mmol/L
Millimoles	Mmol
Milli-equivalent	mEq
Milli-equivalents per liter	mEq/L
Milligrams	Mg
Milligrams per specimen	mg/spec
Millimeters of mercury	mmHg
Milliunits per gram	mU/g
Milli-international units per liter	mIU/g
Milliliters	mL
Millimeters	Mm
Milliunits per liter	mU/L
Milliosmoles per kilogram of water	mOsm/Kg water
Milliunits per liter	mU/L
Minute(s)	Min
Month(s)	Mo
Nanograms per deciliter	ng/dL
Nanograms per liter	ng/L
Nanograms per milliliter	ng/mL
Nanomoles	Nmol
Nanomoles per liter	nmol/L
Optical density	OD
Potential of Hydrogen	pH
Picograms	Pg
Pictograms per milliliter	pg/mL
Picomoles per liter	pmol/L
Seconds	Sec
Units per liter	U/L
Units per milliliter	U/mL
Percent volume	% vol
/24 hours	/24 h
/high power field	/hpf
/low power field	/lpf
/microliter	/mcL
/specimen	/spec
Years	y

REFERENCES

http://www.mayomedicallaboratories.com/test catalog/appendix/measurement.html.
http://www.webmd.com/a-to-z-guides/tc/lab-test-results-units-of-measurement-topic-overview.

Appendix 2

List of Reportable Diseases

Uzma Aamir, National Institute of Health, Islamabad

ANNEXURE: REPORTABLE DISEASES

The Federal Ministry of National Health Services, Regulations and Coordination (NHS, R&C), notified a formal list of following Priority Diseases along with Zoonotic Priority Diseases for surveillance and Response in Pakistan in December 2017. At present, the diseases in the list are considered reportable/notifiable as well.

1. PRIORITY DISEASES

Tuberculosis	Enteric Fever
Measles	Neonatal Tetanus
Hemorrhagic fevers (Including CCHF)	Rabies
Hepatitis B and C	Meningococcal Meningitis
Malaria	Hepatitis A, E, and acute unspecified
Polio and AFP	Anthrax
Severe Acute Respiratory Infections (SARI)	Pertussis
Cholera	Diphtheria
Diarrhea outbreaks	Visceral Leishmaniasis
HIV/AIDS	Viral Meningitis
Botulism	Cutaneous Leishmaniasis
Congenital Rubella Syndrome	Gonorrhoea
Syphilis	Leprosy
Brucellosis	Plague
	Mumps
Dengue/ Dengue Hemorrhagic Fevers/ Dengue Shock Syndrome	Bacterial Meningitis (unspecified, not meningococcal)
Encephalitis (Japanese, Unknown etiology, arbovirus)	Nosocomial Infections (Surgical site infection, neonatal sepsis)

2. ZOONOTIC PRIORITY DISEASES

Influenza
Brucellosis
Rabies
Salmonellosis
Crimean Congo Hemorrhagic Fever (CCHF)
Anthrax

OLD CLASSIFICATION OF DISEASES NOTIFIABLE TO THE OIE

List A

Transmissible diseases that have the potential for very serious and rapid spread, irrespective of national borders, that are of serious socio-economic or public health consequence and that are of major importance in the international trade of animals and animal products.

- Foot and mouth disease
- Swine vesicular disease
- Peste des petits ruminants
- Lumpy skin disease
- Bluetongue
- African horse sickness
- Classical swine fever
- Newcastle disease
- Vesicular stomatitis
- Rinderpest
- Contagious bovine pleuropneumonia
- Rift Valley fever
- Sheep pox and goat pox
- African swine fever
- Highly pathogenic avian influenza

List B

Transmissible diseases that are considered to be of socio-economic and/or public health importance within countries and that are significant in the international trade of animals and animal products.

Multiple species diseases

- Anthrax
- Aujeszky's disease
- Echinococcosis/hydatidosis
- Heartwater
- Leptospirosis
- New world screwworm (Cochliomyia hominivorax)
- Old world screwworm (Chrysomya bezziana)
- Paratuberculosis
- Q fever

- Rabies
- Trichinellosis

Lagomorph diseases

- Myxomatosis
- Rabbit hemorrhagic disease
- Tularemia

Cattle diseases

- Bovine anaplasmosis
- Bovine babesiosis
- Bovine brucellosis
- Bovine cysticercosis
- Bovine genital campylobacteriosis
- Bovine spongiform encephalopathy
- Bovine tuberculosis
- Dermatophilosis
- Enzootic bovine leukosis
- Haemorrhagic septicaemia
- Infectious bovine rhinotracheitis/infectious pustular vulvovaginitis
- Malignant catarrhal fever
- Theileriosis
- Trichomonosis
- Trypanosomosis (tsetse-transmitted)

Other List B diseases

- Leishmaniasis

Sheep and goat diseases

- Caprine and ovine brucellosis (excluding B. ovis)
- Caprine arthritis/encephalitis
- Contagious agalactia
- Contagious caprine pleuropneumonia
- Enzootic abortion of ewes (ovine chlamydiosis)
- Maedi-visna
- Nairobi sheep disease
- Ovine epididymitis (Brucella ovis)
- Ovine pulmonary adenomatosis

- Salmonellosis (S. abortusovis)
- Scrapie

Fish diseases

- Epizootic haematopoietic necrosis
- Infectious haematopoietic necrosis
- Oncorhynchus masou virus disease
- Spring viraemia of carp
- Viral hemorrhagic septicemia

Swine diseases

- Atrophic rhinitis of swine
- Enterovirus encephalomyelitis
- Porcine brucellosis
- Porcine cysticercosis
- Porcine reproductive and respiratory syndrome
- Transmissible gastroenteritis

Mollusk diseases

- Bonamiosis (Bonamia exitiosus, B. ostreae, Mikrocytos roughleyi)
- Marteiliosis (Marteilia refringens, M. sydneyi)
- Mikrocytosis (Mikrocytos mackini)
- MSX disease (Haplosporidium nelsoni)
- Perkinsosis (Perkinsus marinus, P. olseni/atlanticus)

Equine diseases

- Contagious equine metritis
- Dourine
- Epizootic lymphangitis
- Equine encephalomyelitis (Eastern and Western)
- Equine infectious anaemia
- Equine influenza
- Equine piroplasmosis
- Equine rhinopneumonitis
- Equine viral arteritis
- Glanders
- Horse mange
- Horse pox

- Japanese encephalitis
- Surra (Trypanosoma evansi)
- Venezuelan equine encephalomyelitis

Avian diseases

- Avian chlamydiosis
- Avian infectious bronchitis
- Avian infectious laryngotracheitis
- Avian mycoplasmosis (M. gallisepticum)
- Avian tuberculosis
- Duck virus enteritis
- Duck virus hepatitis
- Fowl cholera
- Fowl pox
- Fowl typhoid
- Infectious bursal disease (Gumboro disease)
- Marek's disease
- Pullorum disease
- Crustacean diseases
- Taura syndrome
- White spot disease
- Yellowhead disease

Bee diseases

- Acariosis of bees
- American foulbrood
- European foulbrood
- Nosemosis of bees
- Varroosis

Appendix 3

Sample Job Description

Faisal Hanif, Bahria University Medical College; Umar Khurshid, Combined Military Hospital, Khuzdar Cantt

The common dictum states that “if you fail to plan, you plan to fail”. This might be the simplest words related to a specific job description – essentially meaning what you ought to do in a certain position; hence not doing it amounting to non-delivery and thus detailing the very purpose of the existence of a particular vacancy.

In a work place this set of what is ought to be done is known as JD – Job description. It is a document which is a must for the new employee to orient and familiarize to the needs and demands of a particular job. The script is written in affirmative to mandate the necessary requirements rather than options. The title or position of the individual is mentioned at the outset which is based on certain educational standards or working experience. It is written by an individual with sufficient idea about the nature of the specific job and its intricacies. Review and authorization again shall be done by a person having in-depth analysis of the need of the position and its requirements. The duties of the job description shall outline the minimum essential responsibilities, necessary works, practices and behaviors expected out of an individual in a workplace; and hence can be held accountable for missing those out. These duty statements shall begin with an action verb. The main responsibilities shall be restricted to 3-5; which can be subdivided into further sections depending on the complexity of the job. The responsibilities tasked shall be according to the educational background, training, time and resources allocated to the individual in the setup and shall be synchronous with the pay package. The individual, shall be authorized to certain decision making, has the understanding or is given enough training during induction required for the safe and smooth operation of the particular job. It shall act as a guideline where to start and where to finish within a certain responsibility. It shall give an account of the responsibility chain as to which individual/group of individuals, one is responsible for and how one reports up the channels.

The individual shall sign it and keep in a documented place readily retrievable for audits and verification. The document shall be numbered within the section of the department and the individual mentioned in the JD be listed in the organogram of the section/department. It shall be prepared by a section head, reviewed by a peer and vetted by the departmental head and shall be mandatorily reviewed after a certain period.

HEADINGS FOR INDIVIDUAL JOB DESCRIPTION

Title of JD
Written by
Reviewed by
Authorized by

Date of implementation
Date of revision
Channel of reporting
Responsibilities
Bibliography

Document Information

Category	Information
Document Title	Job Description of Laboratory Tech-1
Version	00
Document ID No	ABS-GHI-MICRO-JD-02
Author(s)	
Reviewer(s)	
Approver(s)	
Creation Date	
Issue Date	
Effective Date	
Control Status	Controlled
Distribution: Issuance / Withdrawal	1. Individual 2. QMR (soft copy)
Disclaimer	This document contains confidential information. Do not distribute this document without prior approval from ----------

Document Revision History

Author(s)	Date	Version	Description

1. Reports to: This position will report to _____
2. Responsibilities:
   - At least two lab technicians will be detailed in each section of the lab like Chemical Pathology, Hematology and one in Microbiology.
   - They will carry out the test to their utmost abilities and according to SOP.
   - They should be a model of discipline and should be cooperative and helpful in dealing with patients.
   - They will keep their equipment neat and clean and will handle them gently and carefully.
   - They will clean and dry all glassware.
   - All the sample and investigation forms received or collected will be checked for their correctness (patient's data and computer ID No). Any discrepancy found later regarding the particulars of the patient or quality of sample would be the fault of that concerned technician and he/she would be responsible for the consequences.
   - The technician receiving the sample from the ward at dispatch section of reception will sign (with date and time) the dispatch register of ward after being satisfied with quantity and quality of the samples.

- The technician will enter correctly the patient's data and lab tests in the computer. Then label the container with the computer ID.
- For any doubt, pathologist will be informed, and fresh sample will be asked from the ward/department without any delay.
- All abnormal findings / doubtful result will be verified from the concerned pathologist before the final report is prepared.
- All technicians, working in any section will keep themselves aware of methodologies used in other section as well.
- Will also be responsible to see that no unauthorized person enters the department

Appendix 4

Work Place Hazard Identification

Part A: Section 2a. Workplace Hazards identification

Using tick boxes identify all hazards associated with workplace, system of work, equipment and substances used. Each of these hazard categories corresponds to information available on the CSIRO OHSE index http://www.csiro.au/services/humanres/essentials/safely/OHSMSIndex.htm

Refer to this index for further information and control strategies on each of the hazards listed below.

Mechanical (Plant)		7. Biological	
1.1 Vehicles, transport		7.1 Biological materials (refer to Part D)	
1.2 Plant, machinery, equipment in		7.2 Biological materials (refer to Part D)	
Motion		Involves GMO's	
1.3 Compression/tension/stored energy		7.3 Allergens / sensitization	
1.4 Noise		7.4 Irritants	
1.5 Vibration		7.5 Genotoxins (mutagens, teratogens)	
1.6 Firearms		7.6 Zoonoses (refer to Part D)	
1.7 Pressure equipment (high/vacuum)		7.7 Handling of small animals	
1.8 Tools, sharps, cutting implements		7.8 Handling of large animals	
		7.9 Handling of human samples (refer to part D)	
2. Radiation		8. Chemical /Hazardous Substances	
2.1 Ionizing (refer to part C1)		8.1 Carcinogens	
2.2 Ultraviolet (refer to Part C2)		8.2 Sensitizing agents	
2.3 Infrared (refer to part C2)		8.3 Corrosive/oxidizing agents	
2.4 Laser (refer to part C2)		8.4 Irritants	
2.5 Radiofrequency (refer to part C2)		8.5 Genotoxins (mutagens, teratogens)	
2.6 Electromagnetic field (refer to part C2)		8.6 Toxic/harmful substances	
2.7 Extremely low frequency (refer Part C2)		8.7 Solvents	
3. Fire and explosion		8.8 Generation of dusts, vapours, fumes etc.	
3.1 Flammable substances		8.9 Asbestos	

3.2 Explosives	☐		
		9. Gases	☐
4. Temperature	☐	9.1 Flammable	☐
4.1 High temperature materials	☐	9.2 Asphyxiant inert gas	☐
4.2 Cryogenic fluids	☐	9.3 Toxic gas	☐
		9.4 Gas cylinders / tanks	☐
5. Hazardous Environments	☐	9.5 Pressurized lines	☐
5.1 Confined spaces	☐		
5.2 Working at heights	☐	10. Personal	☐
5.3 Working at sea or in water bodies	☐	10.1 Manual handling incl striking & grasping	☐
5.4 Heat/cold stress	☐	10.2 Slips, trips, falls	☐
		10.3 Fixed posture, e.g. microscopy	☐
6. Electrical	☐	10.4 Repetitive and/or overuse movements,	☐
6.1 High voltage equipment	☐	e.g. keyboarding, pipetting	☐
6.2 Live electrical equipment	☐	10.5 Pressure (diving/altitude)	☐
6.3 Static charge	☐	10.6 Working alone	☐
	☐	10.7 Field work	☐
	☐	10.8 Mental stress	☐
	☐	10.9 Overseas travel /work (vaccinations)	☐
	☐	10.10 Engulfment e.g. in sand	☐

Appendix 5

Material Safety Data Sheet

Faisal Hanif, Bahria University Medical College; Umar Khurshid, Armed Forces Institute of Pathology, Rawalpindi

A Material Safety Data Sheet (MSDS) is a document that contains information on the potential hazards (health, fire, reactivity and environmental) and how to work safely with the chemical product. It is an essential starting point for the development of a comprehensive health and safety program. It also contains information on the use, storage, handling and emergency procedures all related to the hazards of the material. The MSDS contains much more information about the material than the label. MSDSs are prepared by the supplier or manufacturer of the material. It is intended to tell what the hazards of the product are, how to use the product safely, what to expect if the recommendations are not followed, what to do if accidents occur, how to recognize symptoms of overexposure, and what to do if such incidents occur.

INFORMATION ON MSDS

There are nine categories of information that must be present on an MSDS. These categories are specified in the Controlled Products Regulations and include:

1. Information: product identifier (name), manufacturer and suppliers' names, addresses, and emergency phone numbers.
2. Hazardous Ingredients.
3. Physical Data.
4. Fire or Explosion Hazard Data.
5. Reactivity Data: information on the chemical instability of a product and the substances it may react with.
6. Toxicological Properties: health effects.
7. Preventive Measures.
8. First Aid Measures.
9. Preparation Information: who is responsible for preparation and date of preparation of MSDS.

The MSDS includes information such as the properties of each chemical; the physical, health, and environmental health hazards; protective measures; and safety precautions for handling, storing, and transporting the chemical.

PRODUCT INFORMATION

This section identifies the chemical on the MSDS as well as the recommended uses. It also provides the essential contact information of the supplier. The required information consists of:

- Product identifier used on the label and any other common names or synonyms by which the substance is known.
- Name, address, phone number of the manufacturer, importer, or other responsible party, and emergency phone number.
- Recommended use of the chemical (e.g., a brief description of what it actually does, such as flame retardant) and any restrictions on use (including recommendations given by the supplier).

HAZARD IDENTIFICATION

This section identifies the hazards of chemicals presented on the MSDS and the appropriate warning information associated with those hazards (see Appendix 4). The required information consists of:

- The hazard classification of the chemical (e.g., flammable liquid, category).
- Hazard statement.
- Hazard symbols (e.g., skull and crossbones, flame).
- Precautionary statement(s).
- Description of any hazards not otherwise classified.
- For a mixture that contains an ingredient(s) with unknown toxicity, a statement describing how much (percentage) of the mixture consists of ingredient(s) with unknown acute toxicity.

INGREDIENTS

This section identifies the ingredient(s) contained in the product indicated on the MSDS, including impurities and stabilizing additives. This section includes information on substances, mixtures, and all chemicals where a trade secret is claimed. The required information consists of:

Substances

- Chemical name.
- Common name and synonyms.
- Impurities and stabilizing additives, which must also be classified, and which contribute to the classification of the chemical.
- Mixtures.
- Same information required for substances.
- The chemical name and concentration (i.e., exact percentage) of all ingredients which are classified as health hazards and are:
    - Present above their cut-off/concentration limits; or
    - Present a health risk below the cut-off/concentration limits.
- The concentration (exact percentages) of each ingredient must be specified except concentration ranges may be used in the following situations:
    - A trade secret claim is made;
    - There is batch-to-batch variation; or
    - The MSDS is used for a group of substantially similar mixtures.

Chemicals where a trade secret is claimed

- A statement that the specific chemical identity and/or exact percentage (concentration) of composition has been withheld as a trade secret is required.

FIRST AID

This section describes the initial care that should be given by untrained responders to an individual who has been exposed to the chemical. The required information consists of:

- Necessary first-aid instructions by relevant routes of exposure (inhalation, skin and eye contact, and ingestion).
- Description of the most important symptoms or effects, and any symptoms those are acute or delayed.
- Recommendations for immediate medical care and special treatment needed, when necessary.

FIREFIGHTING

This section provides recommendations for firefighting caused by a chemical. The required information consists of:

- Recommendations of suitable extinguishing equipment, and information about extinguishing equipment that is not appropriate for a particular situation.
- Advice on specific hazards that develop from the chemical during the fire, such as any hazardous combustion products created when the chemical burns.
- Recommendations on special protective equipment or precautions for firefighters.

ACCIDENTAL RELEASE

This section provides recommendations on the appropriate response to spills, leaks, or releases, including containment and cleanup practices to prevent or minimize exposure to people, properties, or the environment. It may also include recommendations distinguishing between responses for large and small spills where the spill volume has a significant impact on the hazard. The required information may consist of recommendations for:

- Use of personal precautions (such as removal of ignition sources or providing sufficient ventilation) and protective equipment to prevent the contamination of skin, eyes, and clothing.
- Emergency procedures, including instructions for evacuations, consulting experts when needed, and appropriate protective clothing.
- Methods and materials used for containment (e.g., covering the drains and capping procedures).
- Cleanup procedures (e.g., appropriate techniques for neutralization, decontamination, cleaning or vacuuming; adsorbent materials; and/or equipment required for containment/clean up).

STORAGE AND HANDLING

This section provides guidance on the safe handling practices and conditions for safe storage of chemicals. The required information consists of:

- Precautions for safe handling, including recommendations for handling incompatible chemicals, minimizing the release of the chemical into the environment, and providing advice on general hygiene practices (e.g., eating, drinking, and smoking in work areas is prohibited).
- Recommendations on the conditions for safe storage, including incompatibilities. Provide advice on specific storage requirements (e.g., ventilation requirements).

PERSONAL PROTECTION

This section indicates the exposure limits, engineering controls, and personal protective measures that can be used to minimize worker exposure. The required information consists of:

- OSHA Permissible Exposure Limits (PELs) and any other exposure limit used or recommended by the chemical manufacturer, importer, or employer preparing the safety data sheet, where available.
- Appropriate engineering controls (e.g., use local exhaust ventilation, or use only in an enclosed system).
- Recommendations for personal protective measures to prevent illness or injury from exposure to chemicals, such as PPE (e.g., appropriate types of eye, face, skin or respiratory protection needed based on hazards and potential exposure).
- Any special requirements for PPE, protective clothing or respirators (e.g., type of glove material, such as PVC or nitrile rubber gloves; and breakthrough time of the glove material).

PHYSICAL AND CHEMICAL PROPERTIES

This section identifies physical and chemical properties associated with the substance or mixture. The minimum required information consists of:

- Appearance (physical state, color, etc.);
- Upper/lower flammability or explosive limits;
- Odour;
- Vapour pressure;
- Odour threshold;
- Vapour density;
- pH;
- Relative density;
- Melting point/freezing point;
- Solubility(ies);
- Initial boiling point and boiling range;
- Flash point;
- Evaporation rate;
- Flammability (solid, gas);

- Partition coefficient: n-octanol/water;
- Auto-ignition temperature;
- Decomposition temperature; and
- Viscosity.

The MSDS may not contain every item on the above list because information may not be relevant or is not available. When this occurs, a notation to that effect must be made for that chemical property.

STABILITY

This section describes the reactivity hazards of the chemical and the chemical stability information. This section is broken into three parts: reactivity, chemical stability, and other. The required information consists of:

Reactivity

- Description of the specific test data for the chemical(s). This data can be for a class or family of the chemical if such data adequately represent the anticipated hazard of the chemical(s), where available.

Chemical Stability

- Indication of whether the chemical is stable or unstable under normal ambient temperature and conditions while in storage and being handled.
- Description of any stabilizers that may be needed to maintain chemical stability.
- Indication of any safety issues that may arise should the product change in physical appearance.

Other

- Indication of the possibility of hazardous reactions, including a statement whether the chemical will react or polymerize, which could release excess pressure or heat, or create other hazardous conditions. Also, a description of the conditions under which hazardous reactions may occur.
- List of all conditions that should be avoided (e.g., static discharge, shock, vibrations, or environmental conditions that may lead to hazardous conditions).
- List of all classes of incompatible materials (e.g., classes of chemicals or specific substances) with which the chemical could react to produce a hazardous situation.

TOXICOLOGY INFORMATION

This section identifies toxicological and health effects information or indicates that such data are not available. The required information consists of:

- Information on the likely routes of exposure (inhalation, ingestion, skin and eye contact). The MSDS should indicate if the information is unknown.
- Description of the delayed, immediate, or chronic effects from short- and long-term exposure.
- The numerical measures of toxicity [e.g., acute toxicity estimates such as the LD50 (median lethal dose) - the estimated amount of a substance expected to

kill 50% of test animals in a single dose].

- Description of the symptoms: This description includes the symptoms associated with exposure to the chemical including symptoms from the lowest to the most severe exposure.

SAMPLE MSDS DATA SHEET

Sample MSDS data sheet can be downloaded from the following links:

https://www.msdsonline.com/files/pdfs/content-offers/class_3_acetone_sample_sds_us.pdf

https://www.msdsauthoring.com/msds-safety-data-sheet-chemicals-samples-msds-examples-sds

REFERENCES

https://osha.gov/oilspills/msds.html.
http://www.osha.gov/dsg/hazcom/index.html.

Appendix 6

Important Contacts

Islamabad
National Institute of Health Chak Shahzad, Islamabad, 45500 Phone: (051) 9255117, 9255110-14 edofficenih@gmail.com
Pakistan Academy of Sciences 3 Constitution Ave, G-5/2, Islamabad Phone: (051) 9225159 president@paspk.org
Pakistan National Accreditation Council (PNAC) Ground Floor, 1-C Constitution Avenue, Opposite Prime Minister Office, G-5/2 Islamabad, Pakistan Phone: (051) 9209507 Fax No. (057) 9209510 info@pnac.org.ok
Pakistan Institute of Medical Sciences (PIMS) Ibn-e-Sina Rd, G-8/3, Islamabad Phone: (051) 9261170, 9260500 Fax: 9260724
PCSIR Head Office 1-Constitution Avenue, G-5/2, Islamabad Phone: (051) 9225395-99, Fax:9225372
Department of Diagnostic Laboratories Nuclear Medicine, Oncology and Radiotherapy Institute (NORI) G-8/1, Hanna Road, Islamabad Phone: (051) 9260611-15
Excel Labs 110 Fazal-ul-Haq Road, Reshi Building, Blue Area, Islamabad Phone: (051) 8311000
Islamabad Diagnostic Centre (IDC) 13-A, Khayal Plaza, Main Kohistan Road, F-8 Markaz, Islamabad Phone: (051) 2251212
Kulsum International Hospital (KIH) Laboratory Kulsum Plaza, 2020-Blue Area, Islamabad Phone:+92 (51) 8446666
Shifa International Hospital Laboratory Pitras Bukhari Rd, H-8/4, Islamabad Phone: (051) 4603666

Punjab
Armed Forces Institute of Pathology (AFIP) Rawalpindi Cantt Phone: 051-5176419
Al-Razi Healthcare (Pvt) Ltd Laboratory 9-Gulshan Block, Allam Iqbal Town, Lahore Phone: +92 30 08 50 5483
Centre for Excellence in Molecular Biology 87 West Canal Bank Road, Thokar Niazbaig University of the Punjab, Lahore Phone: (042) 35293141
Chughtai Labs Jail Road, Lahore Phone: (042) 111-255-790
Indus Clinical Laboratories 99 Anwer, Tower Main Boulevard, Shadman, Lahore Lahore, 54000 Phone: (042) 37420666
Pathology Laboratory Services Institute of Medical Sciences, Lahore Phone: (042) 99205514
Shaukat Khanum Hospital Laboratory Block R3, Phase 2, Johar Town, Lahore Phone: (042) 3590500
University of Health Sciences Khayaban-e-Jamia Punjab, Block D New Muslim Town, Lahore Phone: (042) 111 333 366
University of Veterinary and Animal Sciences (UVAS) Laboratory Syed Abdul Qadir Jillani (Outfall) Road Lahore, Kasur, Punjab, 54000 Phone: (042) 99211374
Sindh
Aga Khan University Hospital Stadium Road, P.O. Box 3500, Karachi, 74800 Phone: (021) 111-911-911/021-34930051 Fax: +92 21 34934294, 34932095 akuh.information@aku.edu
Bahria University Medical & Dental College DHA Phase-II, Karachi Phone: (021) 35319491-9 Info.bumdc@bahria.edu.pk

Dow Diagnostic Reference and Research Laboratory (DDRRL) Dow University of Health Sciences (DUHS) Gulzar-E-Hijri KDA Scheme 35, Karachi Phone: (021) 9261488, 99232660
Dr. Essa's Laboratory & Diagnostic Centre B-122 Blue Building, Shahrah-e-Jahangir Rd, Scheme 24, Block H, North Nazimabad Town, Karachi Phone: (021) 36626125
International Center for Chemical and Biological Sciences University of Karachi, 75270 UAN: 111-222-292 Phone: (021) 99261701-2, 34824930, 4824901-02
Isra University Laboratory New Hala, Mirpur Khas Rd Link, Hyderabad Phone: (022) 2030181
Karachi Institute of Medical Sciences Malir Cantonment, Karachi Phone: (021) 99247501
Liaquat National Medical College Stadium Road, Liaquat National Hospital, Karachi Phone: (021) 111 456 456
Memon Medical Institute (MMI) Laboratory 12-F/8, Ghazi Salahuddin Road, Haider Bux Gabol Road Safora Goth, KDA, Karachi Phone: (021) 34937474, 021-34691147, 021-48506777
PNS Shifa Hospital Laboratory Main Korangi Road, Near Kala Pul, Karachi Phone: (021) 48506500
Sindlab Hilal-e-Ahmer House, Main Clifton Road Block 7, Clifton, Karachi, 75600 Phone: (021) 35373662
Tabba Heart Institute Laboratory St-1, Federal B Area, Azizabad Block 2, Gulberg Town, Karachi, 75950 Phone: (021) 111 844 844
University of Karachi Main University Road, Karachi, 75270 Phone: (021) 99261300
Ziauddin Medical University Laboratory Ziauddin Chowrangi, Allama Rasheed Turabi Road, Block-B Near North Nazimabad Town, Karachi, 74600 Phone: (021) 35862937

Khyber Pakhtunkhwa
Forensic Science Laboratory Peshawar 29 Sector B1, Ring Road, Phase 5, Hayatabad, Peshawar Phone: (091) 9217394
Khyber Medical University Phase V, Hayatabad, Peshawar Phone: (091) 9217703, 9217696
Lady Reading Hospital Soekarno Rd, Pipal Mandi, Peshawar Phone: (091) 9211441/ 091924400/091-9211430
Post Graduate Medical Institute Peshawar Phase-4, Hayatabad, Peshawar Phone: (091) 9217190
Sina Labs Opposite Hayatabad Medical Complex, Phase-4, Hayatabad, Peshawar Phone: (091) 5825046
University of Peshawar Old Jamrud Road, Qadir Abad, Peshawar Phone: (091) 9216701
Balochistan
Bolan University of Medical & Health Sciences Laboratory Brewery Rd, Quetta, 87300 Phone: (081) 9213070/ 081-9213030
University of Balochistan Quetta Phone: (081) 9211008
Azad Jammu & Kashmir
AIMS Hospital Laboratory Muzaffarabad Phone: (058224) 39306
Azad Jammu Kashmir Medical College Jalalabad Stadium Rd, Domail, Muzaffarabad Phone: (058229) 20527
CMH Muzaffarabad Laboratory Muzaffarabad Phone: (058229) 20451
Mirpur University of Science and Technology Mirpur Phone: (058279) 61037
Mohi-ud-Din Islamic Medical College Mirpur

Appendix 7

Shipping Information

List of Infectious Substances: Category A

The list of Category A infectious substances is provided below for reference as per WHO Guidance on regulations for the Transport of Infectious Substances September 2005, Communicable Disease Surveillance.

SUGGESTIVE EXAMPLES OF INFECTIOUS SUBSTANCES	
UN Identification Number & Right Shipment Name UN 2814 Infectious substances affecting humans	
Anthrax Bacillus (culture specimen) *Burkholderia mallei* (live cultures) *Clostridium botulinum* *Coxiella burnetti* (cultures) Dengue Virus (cultures) *Escherichia coli,* verotoxigenic Ebola virus Hantaan virus Hendra virus Herpes B virus Highly pathogenic avian influenza virus Machupo virus Mycobacterium tuberculosis Poliovirus *Rickettsia prowazekii* *Shigella dysenteriae* type 1 Variola virus West Nile virus *Yersinia pestis*	*Brucella* species (cultures/specimen) *Burkholderia pseudomallei* (live cultures) *Chlamydia psittaci* – avian strains (cultures) *Coccidioides immitis* (cultures) Crimean-Congo haemorrhagic fever virus Eastern Equine Encephalitis virus *Francisella tularensis* Flexal virus Hantavirus Hepatitis B virus HIV Japanese B Encephalitis virus Monkeypox virus Nipah virus Rabies virus *Rickettsia rickettsiae* Tick-borne encephalitis virus Venezuelan equine encephalitis virus Yellow fever virus
UN 2900 infectious substances affecting animals only	
African Horse Sickness virus Avian Paramyxovirus Type 1 Classical swine fever Lumpy skin disease virus Peste des petits ruminants virus Sheep Pox virus Swine Vesicular Disease virus	African Swine Fever virus Bluetongue virus (Note: deleted by the air mode from 2005) Foot & Mouth Disease *Mycoplasma mycoides* Rinderpest virus Goat Pox virus Vesicular stomatitis

SHIPPING IDENTIFICATION NUMBERS:

UN 2814	Category A infectious substance which can cause disease in humans or both in humans and animals.
UN 2900	Category A infectious substances which can cause disease in animals only.
UN3373	Category B “Biological substance”.
UN 3245	GMOs that do not fulfill the criteria of being an infectious substance

Appendix 8

Equipment Logbook

Nomenclature:
Model:
Installation date:
Period of warranty:
Emergency contact:

Date and Time	Maintenance Performed	Performed by (name and company)	Details of maintenance	Maintenance authorized by:	Remarks

Appendix 9

Incident Notification Form

DATE: _____ TIME: _____

Please complete section 1 & 2 then submit to the Laboratory Manager/concerned In-charge. Keep a copy for personal and laboratory records. Fill all the fields, please write N/A if not applicable.

Section 1: Details of affected personnel

Full Name of the affected person:	
Occupation:	
Phone Number:	
Email:	
CNIC Number:	
First Aid Provider Name (Specify):	

Section 2: Details of incident

Property Damage	
Environmental Damage	
Near Miss	
Personal injury	
Biological Agent involved	

Section 3: Questions

Were there any eyewitnesses?	Name:
	Phone: Email:

Describe the incident/ event in your own words and language; draw a diagram if required on a separate sheet. (Try to write exactly what happened and it must include if any particular microorganism, chemical agent, process or equipment is/are involved).

Details of personal injuries, please describe what, where and severity of injury:

Section 4 Notification of Administration

To be filled out by Supervisor and/or Administration:
Action taken:

Name: _____ Date:

Position: _____ Signature:

Appendix 10

Example of Inventory Sheet

A template for a sample inventory list (information may be modified as per user's need)

Sample Storage Inventory					
Freezer ID/Temperature			NIH/PHLD/VIRO/001 ((-80°C)		
Project/Study Name			NIH-ABC-2017		
Department and Institute			Department of Virology National Institute of Health, Islamabad		
S.No.	**Sample ID**	**Sample Type**	**Sample Volume (µl)**	**Sample Well Position**	**Cryobox No.**
1	NIH-001	serum	100	1	NIH-ABC-001
2	NIH-002	oral fluid	200	2	NIH-ABC-001
3	NIH-003	serum	200	3	NIH-ABC-001
4	NIH-004	Vero-isolate	300	4	NIH-ABC-001
5	NIH-005	blood	200	5	NIH-ABC-001
6	NIH-006	serum	100	6	NIH-ABC-001
7	NIH-007	serum	100	7	NIH-ABC-001
8	NIH-008	serum	100	8	NIH-ABC-001
9	NIH-009	serum	100	9	NIH-ABC-001
10	NIH-010	serum	100	10	NIH-ABC-001
11	NIH-011	serum	100	11	NIH-ABC-001
12	NIH-012	serum	100	12	NIH-ABC-001
13	NIH-013	serum	100	13	NIH-ABC-001
14	NIH-014	serum	100	14	NIH-ABC-001
15	NIH-015	serum	100	15	NIH-ABC-001
16	NIH-016	serum	100	16	NIH-ABC-001
17	NIH-017	serum	100	17	NIH-ABC-001
18	NIH-018	serum	100	18	NIH-ABC-001
19	NIH-019	serum	100	19	NIH-ABC-001
20	NIH-020	serum	100	20	NIH-ABC-001
21	NIH-021	serum	100	21	NIH-ABC-001
22	NIH-022	serum	100	22	NIH-ABC-001
23	NIH-023	serum	100	23	NIH-ABC-001
24	NIH-024	serum	100	24	NIH-ABC-001
25	NIH-025	serum	100	25	NIH-ABC-001
26	NIH-026	serum	100	26	NIH-ABC-001
27	NIH-027	serum	100	27	NIH-ABC-001
28	NIH-028	serum	100	28	NIH-ABC-001
29	NIH-029	serum	100	29	NIH-ABC-001

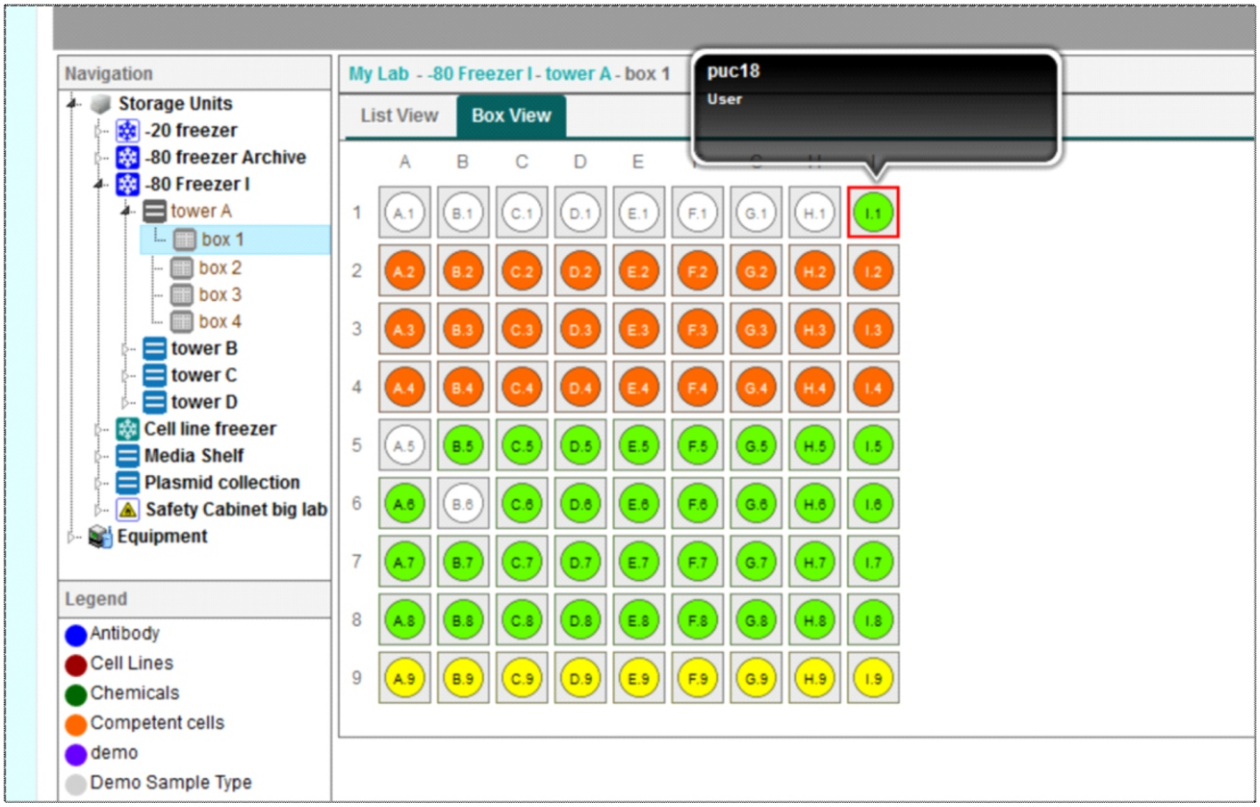


FIGURE A10-1. Computer view of a LIMS system showing a box of vials and information for each tube

Appendix 11

SOPs for Laboratory Procedures

SOME EXAMPLES

Category	Information
Document Title	SOP for Stool RE
Version	
Document ID No	
Author(s)	
Reviewer(s)	
Approver(s)	
Creation Date	
Issue Date	
Effective Date	
Control Status	
Distribution: Issuance / Withdrawal	
Disclaimer	

Author(s)	Date	Version	Description

STOOL ROUTINE EXAMINATION

1. Collection of Specimen

- Stool specimen should not be mixed with urine.
- The specimen should be at least 4 ml in quantity.
- If the stool contains mucus and blood, then it should be collected and sent to the laboratory preferably within one hour.

2. Physical examination

- **a. Color**
  - Normal color of faeces (brown) = Stercobilinogen
  - Infant's stool color = Yellow (No stercobilinogen)
  - Diarrhoeal stool = Green

- Obstructive jaundice = Clay coloured
- Chlorophyll rich food (Vegs) = Green
- Upper GIT bleeding = Black
- Lower GIT bleeding = Red

- **b. Odour:**
  - Normal odour of stool is because of indole with skatole.
  - Offensive faeces in Amoebic dysentery.
- **c. Consistency**:
  - Normal faeces are formed or semi formed.
    - Faeces can be in liquid, semiliquid, semisolid and foamy.
  - Hard faeces can be seen in in constipation and loose faeces in diarrhea.
  - Diarrheal faeces mixed with blood and mucus are seen in amoebic dysentery, carcinoma of large intestine, and typhoid fever.
  - Diarrheal faeces mixed with pus and mucus are seen in:
    - Bacillary dysentery
    - Regional enteritis
    - Ulcerative colitis
  - Paste like and frothy faeces are seen in:
    - Sprue
    - Pancreatic insufficiency
    - Malabsorption Syndromes
    - Rice water faeces: in cholera

3. Parasites:

- Some of the parasites can be seen with naked eye like *Ascaris lumbricoides*, *Entrobius vermicularis* and Segments of *Tenia saginata*

4. Reaction (pH)

- Normal stool has either neutral or weekly alkaline pH.
- The alkaline faeces are seen if meat diet has been taken. If the diet is rich in carbohydrate or fat, then the reaction is acidic.
- In Amoebic dysentery, the reaction is acidic reaction.
- In bacillary dysentery the reaction is alkaline due to protein break down.
- Lactose intolerance in infants = acidic (fermentation of lactose).

5. Microscopic Examination (Saline Preparation)

- Place a drop of Normal saline on the glass slide.
- With the help of loop pick up small amount of faeces and mix in saline drop (Faecal matter selected should contain blood and mucus in dysentery).
- Place or cover slip and see under x 10 objective and then under high power x 40 objective.
- For microscopic examination, following is to be seen:

- Food residues (digested, undigested muscle particles, fat globules and cellulose residues)
- Cells (RBCs, WBCs & epithelial cells)
- Crystals (Triple phosphate, calcium oxalate, cholesterol and charcot Leyden crystals)
- Ova (*Ascaris lumbricoides, E. vermicularis, A. duodenale*, etc.)
- Trophozoites (Amoeba)
- Cysts (Giardia, Amoeba)
- Foreign bodies (Hair and wool etc.)

6. Methylene blue staining: Used to demonstrate the pus cells.

Gram Staining of Faeces

Gram stain is required in certain conditions like:

Suspected infection in campylobacter, clostridium, candida or other fungi:

- Campylobacter is Gram negative curved rods
- Clostridium is Gram positive rods
- Candida is spores/budding seen

8. Motility

- Hanging drop method for the *Vibrio cholera* infection.
- Method is applied directly from stool specimen or alkaline peptone water if specimen is brought in it.

9. Procedure

- A slide with well is best used for this purpose.
- The faecal suspension should be placed in the centre of cover slip and inverted over the well.
- Margins of drop are examined under the microscope to see the motility.

SOP FOR BLOOD CP

Category	Information
Document Title	**SOP of Blood CP**
Version	
Document ID No	
Author(s)	
Reviewer(s)	
Approver(s)	
Creation Date	
Issue Date	
Effective Date	
Control Status	
Distribution: Issuance / Withdrawal	
Disclaimer	

Author(s)	Date	Version	Description

Blood CP

1. Procedure: The purpose of this SOP is to explain how to conduct the test procedure of blood complete picture.

2. Scope: Applicable to lab ABC only.

3. Responsibility: Medical Officer in-charge of Lab is responsible for effective implementation of the SOP.

4. Procedures:

- Blood complete picture is one of the most commonly ordered tests by the physicians. The blood is subjected to analysis of 18 parameters using the Sysmex KX-21 semi-automated hematology analyzer. The instrument employs three detector blocks and two kinds of reagents for blood analysis. WBC count is measured by the WBC detector block using the DC detection method. The RBC count and platelets are taken by the RBC detector block, also using the DC detection method. The haemoglobin detector block measures the haemoglobin concentration using the non-cyanide haemoglobin method. Rest of the parameters is calculated. The instrument analyzes the following parameters:
    - Whole WBC (white blood cell) (Analysis principle: DC detection method). WBC count in 1 l
    - Based on the results obtained from the KX-21 the peripheral blood film from the sample is prepared and forwarded to the haematologist when:
        - TLC < 4000 and > 10,000
        - If the TLC >50,000 than dilute the specimen 1:10
        - DLC mixed > 10%
        - Hb < 10 g/dl and > 17.5 g/dl male & 15.5 g/dl in females
        - Platelet count: < 100 and > 600 x 10^9/l
        - MCV < 75 and > 100 fL
        - MP - All cases
        - Oncology - All cases
        - RBC morphology - All the cases
        - Patient having fever
        - RDW >45 fL

5. RETICULOCYTE COUNT: The reticulocytes are immature red cells. These contain thread like structures in the cytoplasm, which consist of ribonucleic acid (RNA). RNA can be stained blue with brilliant cresyl blue or new methylene blue. New methylene blue stains the RNA filaments more deeply and uniformly and is preferred.

- **Reagents and equipment**
  - Reticulocyte stain: 1g of new methylene blue or brilliant cresyl blue dissolved in 100 ml of citrate saline solution (49 mg trisodium citrate dissolved in 100 ml normal saline). Filter the mixture and it is ready for use.
  - Pasture pipette.
  - 75x10 mm test tube.
  - Glass slide and spreader.
  - Microscope.
- **Procedure:**
  - Add 2-3 drops of stain and equal amount of blood in a test tube.
  - Incubate the mixture at 37°C for 15-20 minutes.
  - The cells can be re-suspended by gentle mixing. Prepare smears on glass slides and air dry.
  - The slide can then be examined under a microscope using oil immersion lens.
  - The area of the film where the cells are not distorted or overlapping and the area which has been properly stained should be chosen. Count the reticulocytes and the RBC in the area. The field of counting can be narrowed either by using an eye piece with an adjustable diaphragm or a piece of paper with a central small 4mm square window placed in the eye piece. At least 100 reticulocytes are counted.
  - Percentage of reticulocytes is calculated by the following formula:
    - Number of reticulocytes in 100 fields x 100
    - Total number of RBCs in 100 fields
- **Normal range**
  - Adult (both sexes) 0.2 - 2%
  - Infants 2 - 6%
- **Precautions**
  - Fresh sample should be used for reticulocyte count as their number decreases with storage due to maturation.
  - At least 1000 red cells should be counted.
  - Reticulocytes should not be confused with HbH inclusions found in HbH disease. HbH inclusions stain paler, are dot like and occur in most of the red cells. In doubtful cases prolonging the incubation to 2-4 hours can reduce the reticulocyte count whereas Hb-H inclusions remain unchanged. Heinz bodies also stain with the supravital stains. These appear as small dots present near the cell membrane and should not be confused with reticulocytes.

SOP FOR HAEMATOXYLIN AND EOSIN STAINING

Category	Information
Document Title	Slide staining H&E
Version	
Document ID No	
Author(s)	
Reviewer(s)	
Approver(s)	
Creation Date	
Issue Date	
Effective Date	
Control Status	
Distribution: Issuance / Withdrawal	
Disclaimer	

Author(s)	Date	Version	Description

HAEMATOXYLIN AND EOSIN STAINING

Clinical significance:

It is commonly used for routine histopathology and in diagnostic cytology. Its particular value lies in its ability of imparting proper differentiation to distinguish between different types of connective tissue fibres and matrices, by staining them different shades of red and pink.

Principle:

First, the tissue is cleared of all wax and then dehydrated to facilitate the entry of dyes. The tissue sections are then sequentially exposed to a basic dye e.g. Harris's Haematoxylin and an acid dye e.g. eosin. This stain both basic and acid components of the tissue.

Tissue Processing:

Fixation and processing done according to SOP of tissue processing.

1. Instruments and appliances:

- Microtome for section preparation from blocks.
- Hot air oven for section adhesion to slide.

2. Reagents:

- Haematoxylin 5.0 g
- Alcohol 95% 50 ml

- Ammonium or Potassium Alum 100 g
- Mercuric oxide 2.5 g
- Distilled water 1 litre
- Glacial acetic acid 40 ml

Haematoxylin is dissolved in alcohol and alum in water with the help of heat separately. The two solutions are then mixed. The mixture is then rapidly boiled Bring the mixture rapidly to boil. Then remove from flame and add mercuric oxide. The solution is then reheated for one minute until it becomes dark purple. When it is cooled, the solution is then ready for use. Then add 2-4 ml of Glacial acetic acid per 100 ml of solution if desired.

Acid Alcohol:

It is prepared by mixing one litre of 70% alcohol with 10 ml of conc. Hydrochloric acid.

Ammonia water:

This is prepared by mixing 2-3 ml of strong ammonia with one litre of tap water.

Alcoholic eosin solution:

- Eosin (water voluble) 2 g
- Distilled water 160 ml
- Alcohol 95% 640 ml

Others:

- Xylol
- Absolute alcohol
- Rectified spirit
- Methylated spirit

Staining procedure:

- The sections fixed on a glass slide are put in in xylol for 3 minutes.
- Then it is transferred to absolute alcohol for 3 minutes.
- In next step it is transferred to rectified spirit (80% alcohol) for 2 minutes.
- It is then placed in methylated spirit for 2 minutes.
- The slide is then washed in running water for 1 minute and then put it in Harris haematoxylin for 3-5 minutes.
- The slide is then washed in running water for 30 seconds and the excess dye is washed in 1% acid alcohol by continuous agitation for 15 seconds.
- It is then washed in running water for 30 seconds.
- Give 2-3 dips in ammonia water solution until tissues attain a blue color.
- Wash in running water for 2-3 dips.
- Counter stain with eosin for 2-3 minutes.
- Wash in running tap water for 30 seconds.
- Dehydrate by keeping in increasing concentrations of alcohol (in 70%, 95% and absolute alcohol).
- Clear it in xylol and mount with Canada balsam.

Results and interpretation:

- Nuclei — Bright blue
- Muscle, keratin — Bright pink
- Collagen and cytoplasm — Pale pink
- Erythrocytes — Orange red

Notes and Precautions:

Other haematoxylins like Mayer's haematoxylin may also be used. All have different methods of preparation. The reagents must be checked daily for any deterioration and changed when needed. In the manual method, the xylol and alcohols must be changed daily, haematoxylin once a week, eosin solution and acid alcohol twice a week, and ammonia water daily. This regimen may be modified by the amount of usage. In the automatic stainer, xylol, alcohols, eosin solution and acid alcohol, are changed twice a week. Haematoxylin is changed once in two weeks and ammonia water is changed daily.

Quality Control:

The quality of alcohol available must be checked before use. This can be done by adding 4-5 g of copper sulfate crystals to a Coplin jar containing alcohol. If the colour remains bluish white (unchanged) for about 10 minutes the quality is acceptable. If the colour changes to green the quality of alcohol is unsuitable for processing.

Appendix 12

Definitions

Antibiogram: type of cumulative report prepared by microbiology laboratory to guide the clinicians regarding selection of empiric antimicrobials as per existing trends in antimicrobial resistance.

Biohazard: biological substances that pose a threat to the health of living organisms, primarily that of humans. This can include samples of a microorganism, virus or toxin (from a biological source) that can affect human health.

Bio-incident: irregularities that occur while handling biological agents (pathogenic organisms), including those which have been genetically modified, cell cultures and parasites which can cause any infection, allergy or toxicity. They can be due to human errors or technical failures.

Biological waste (Infectious & Non-Infectious): any material that contains or has been contaminated by a biohazardous agent.

Biorisk: the risk associated with biological materials and/or infectious agents.

Biosafety (aka Biological Safety): as defined by WHO is the containment principles, technologies and practices which are implemented to prevent unintentional exposures to pathogens and toxins, or their accidental release.

Biosafety Level (BSL): refers to the amount of engineering containment located within a laboratory. Different pathogens require different levels of biocontainment.

Biosecurity (aka Biological Security): institutional and personal security measures to prevent the theft or loss of pathogens or toxins for any malicious use.

Category A Biological Material: material that can cause an infectious disease when exposure occurs during transportation.

Category B Biological Material: infectious material which does not meet the criteria for inclusion in Category A.

Chemical Waste: waste that comprises harmful chemicals.

Commissioning: the process to document and validate that quality standards are met during construction of a laboratory facility.

Conflict of Interest: a situation in which a person or organization may be involved in multiple financial, personal, professional, or other activities, and serving one interest could involve working against another.

Continuing Education: a program, within an institution or through independent groups, that allows professionals to keep up to date on their knowledge through training, lectures, etc.

Continuity of Operations Plan: a pre-defined plan that ensures continued performance of essential functions under a broad range of circumstances.

Critical/Panic Values: test result values that are outside the normal range to a degree that may constitute an immediate health threat to the individual or require immediate action on the part of the treating physician.

Cytotoxic Waste: waste generated from protean sources such as manufacturing waste, home care waste, contaminated materials from drug preparation and administration (expired medicines, left-over drugs, returned drugs, syringes, needles, gauzes, vials, packaging).

Dry Laboratory: laboratory that applies computational or analytical research, such as modelling, robotics, etc.

Emergency Operations Plans: course of action developed to mitigate the damage of potential events that could endanger an organization's ability to function. Such a plan should include measures that provide for the safety of personnel and, if possible, property and facilities as well.

Exempt Substances: a sample which does not contain infectious substances, or the substances are not likely to cause disease in animals or humans.

Good Clinical Practices: recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.

Hazardous Waste: any waste that may be hazardous to life including biological waste, chemical waste, radioactive waste, nuclear waste, cytotoxic waste, etc.

Infection Control Office: In charge of monitoring and preventing the spread of infectious agents through protocol development and training.

Infectious Substances: materials which are known or are reasonably expected to contain pathogens.

Infectious Waste: that contains infectious agents, e.g., human blood and blood products, isolation waste, pathological waste, contaminated animal waste, and discarded sharps (broken bottles, needles, scalpels).

Information Management System: the processes that facilitate the collection, storage, organization, retrieval and analysis of data from various sources.

International Health Regulations (IHR): legally binding instrument of international law that aims to assist countries to work together to save lives and livelihoods endangered by the international spread of diseases and other health risks; and avoid unnecessary interference with international trade and travel.

International Standard Organization (ISO): an international standard-setting body composed of representatives from various national standards organizations.

LIS Standards: defines software systems for the appropriate working of clinical laboratories; these LIS systems make up critical component of vital and prompt diagnostic services.

Medical Surveillance Program: the systematic assessment of employees exposed or potentially exposed to occupational hazards. This assessment monitors individuals for adverse health effects and determines the effectiveness of exposure prevention strategies.

Medical/Clinical Waste: the waste material generated in response to medical treatment or biological research on humans and animals.

Material Safety Data Sheet (**MSDS**)**:** a document that contains information on the potential health effects of exposure to chemicals, or other potentially dangerous substances, and on safe working procedures when handling chemical products.

Nonhazardous Waste: any waste without hazardous material.

Non-infectious Waste: any waste that without any infectious agent.

Occupational Health Program: program to identify and control the risks arising from physical, chemical, and other workplace hazards to establish and maintain a safe and healthy working environment along with the monitoring of health of the staff and dealing with any accidental exposure.

Organizational Standards: processes and procedures always defined by the organization that ensure a clear management scheme and efficient laboratory operations.

Pathogen Safety Data Sheet: technical documents that describe the hazardous properties of a human pathogen and provide recommendations for work involving these agents in a laboratory setting.

Pathogen: a microbe including bacteria, rickettsiae, viruses, and fungi, and other pathogenic agents such prions, which are known to cause illness in man or animals. These include parasites as well.

Pathological waste: as any recognizable human or animal body part, organs and tissue.

Personnel Standards: qualities which the clinical laboratory workers must exhibit during the pursuit of their professional duties.

Proficiency Testing: testing of unknown samples sent to a laboratory by regulatory/accrediting bodies to compare the results of participating laboratories.

Public Health Surveillance: the continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice.

Public Health Testing: the laboratory testing of country specific priority diseases and environmental samples as decided by National/ Provincial Authorities.

Quality Assurance: Process used to measure and confirm the quality of a product.

Quality Control: process of ensuring product meet the standards defined by the laboratory, accreditation or regulatory bodies.

Radioactive Waste: waste that contains radioactive material.

Risk Assessment: a process to determine the potential risks of an activity.

Spill Kit: a collection of items, to be used in case of a spill, leak or other discharge of a potential hazardous liquid.

Standard Operating Procedure: describes stepwise the correct method for doing a task explaining all pre-analytic, analytic and post analytic factors which can influence the accuracy and validity of reporting.

Waste Management Plan: the defined plan and protocols for managing waste generated within an institute, hospital or independent laboratory.

Wet Laboratory: laboratory that conducts biological or chemical manipulations and experiments.

IMPORTANT NATIONAL DOCUMENTS

National Laboratory Policy 2017. Available at: https://www.nih.org.pk/wp-content/uploads/2018/06/National-Laboratory-Policy.pdf

National Laboratory Biosafety & Biosecurity Policy 2017. Available at: https://www.nih.org.pk/wp-content/uploads/2018/06/Biosafety-Policy-NLWG.pdf

National Biosafety Rules 2005. Available at: https://www.nti.org/media/pdfs/pakistan_bw_biosafety_rules_1.pdf?_=1339193223&_=1339193223

National Biosafety Guidelines 2005. Available at: http://www.environment.gov.pk/images/PDF/BiosftyGlines2005.pdf

Code of Conduct for Life Scientists 2010

Priority diseases in Pakistan 2017. Available at: https://www.nih.org.pk/wp-content/uploads/2018/11/Notification-of-Priority-Diseases-in-Pakistan.pdf

AMR National Action Plan 2017. Available at: https://www.nih.org.pk/wp-content/uploads/2018/08/AMR-National-Action-Plan-Pakistan.pdf